TEXTBOOK OF

MEDICAL TREATMENT

By Various Authors

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PREFACE TO FIRST EDITION

This book has been written for students and practitioners in the hope that it may fill the therapeutic gap left by the majority of textbooks on general medicine in which, owing to exigencies of space, the section devoted to treatment is often [illegible]

can be put into practice. The following statements, for instance, are frequently made: "vaccines may be of value," "arsenic may be tried," "a well-balanced diet should be given," "the general health should receive attention" Further, it is not uncommon for many drugs and measures recommended by our forefathers to continue to be included in such works year after year in spite of the fact that some of them have been shown to be useless and others are known to be less efficacious than modern substitutes

An attempt has therefore been made by the authors of this book to be [illegible]

indications, contra-indications and dangers of each recommended method or drug are fully discussed

Further, an attempt has been made to indicate why and when certain drugs and methods formerly widely used should no longer be employed for the particular purpose under discussion. From this it follows that the number of drugs advised are considerably fewer than in some books of therapeutics, but this we believe to be wise, for undue reliance on the "bottle of medicine" has tended in the past to obscure and diminish the importance of certain general measures of paramount importance which may be included under the heading "General Management of the Patient," *i.e.*, diet, rest, exercise, nursing, etc, [illegible]

given to the relatives and patient in certain circumstances, and general advice on where and when to send patients to sanatoria, spas or for a change of air and climate. Lastly, the good management of a case frequently requires a knowledge of common-sense psychological principles which are so important in the art of medicine.

It is well recognized that in some diseases where no specific therapy exists a variety of methods of treatment may be advocated by different authorities. In others, even though the general principles of treatment are unanimously approved, yet the details of their practical application may vary widely in different hands. For example, it would be generally admitted that a case of severe diabetes requires insulin, but opinion differs upon the type of insulin to be used, the details of its administration, and upon the quantity of carbohydrate to be allowed in the diet. No attempt has been made in this book to give a comprehensive

[illegible]

[illegible] rational [illegible] methods [illegible] When the procedures are of such a specialized nature as to be outside the scope of the general practitioner, only a brief outline is given

The work is not a small handbook of treatment, nor yet a vast encyclopædia, since there are already a number of such books Neither is it a textbook of pharmacology, since a large portion of the book deals not with drugs but with the "Management of the Case" in the widest sense of the term. It is not concerned with surgery, but includes sections on the treatment of venereal diseases, tropical medicine, some diseases peculiar to infants, common diseases of the skin, industrial diseases and the neuroses. There is, in addition, a section which describes in detail the technique of certain essential medical procedures—such as lumbar puncture, venesection, paracentesis, blood transfusion, oxygen therapy, etc.

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COMMON DISEASES OF THE SKIN

VENEREAL DISEASES

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INFECTIOUS DISEASES

INTRODUCTION

WHEN DISEASE is the result of invasion of the human tissues by bacteria and other micro-organisms, the condition is called an infection. Those infections which are transmitted naturally from one person to another are broadly classed " infectious diseases ". For various reasons, including administrative expediency, a number of these diseases are regarded as the responsibility of special hospitals—the infectious diseases hospitals Although the classification is arbitrary rather than strictly scientific, it accounts for the selection of diseases included in this chapter. It also explains why venereal diseases, tuberculosis, parasitic infestations and tropical diseases are dealt with elsewhere in this book

[illegible] is o[illegible] patie[illegible] bacterial invasion are determined principally by the virulence of the micro- [illegible] defences and cause death in a few hours.

An acute infection may thus be regarded as a struggle between a susceptible [illegible]

effective chemotherapy—that the value of general nursing management is easily overlooked, but it remains of importance, for in the severe case of infection it is still true to say that proper supportive medical and nursing measures increase the likelihood of a successful outcome.

At the outset, it is worthwhile to draw attention to an important contrast between bacterial and viral diseases. In almost all bacterial infections the organism remains mainly extracellular and can thus be reached with comparative ease by substances which are present in the blood stream. Although it is reasonable to assume that there is a temporary stage of viræmia in many of the virus diseases, the causative organism is capable of growth only inside the body cell so that it rapidly becomes inaccessible to the usual methods of treatment. Such localization of the virus in body cells has often occurred by the time the infection becomes manifest, and up to the present no practicable method has been devised of modifying the effect after the cell has been invaded The specific treatment of virus diseases therefore [illegible]

GENERAL MANAGEMENT OF THE FEBRILE STATE

Although pyrexia, arising from interference with the function of the heat regulating centre, is usually a cardinal sign of an infection, in some cases, and

those the most toxic, the temperature may not rise above normal. Wasting due to increased catabolism, dry hot skin, acceleration of the pulse and respiration, coated tongue, anorexia, vomiting and constipation or diarrhœa; headache, restlessness, insomnia and delirium; quantitative and qualitative changes in the urine; all these manifestations are a result of the reactions of the tissues of the host to the effects of the bacterium or its products.

The primary essentials in the general management of the fevered person are (*a*) rest; (*b*) efficient nursing, (*c*) a suitable diet with adequate intake of water; and (*d*) relief of symptoms

Rest.—Confinement to bed is essential as long as the temperature remains elevated, and should be continued for a varying, but not prolonged, period in convalescence Strict bed rest should never be regarded as an end in itself. When there is no obvious contra-indication, walking should be encouraged early. In the young patient it is better to be officially up and properly dressed than to be continually in and out of bed without adequate clothing. In the elderly the real risks of a long period in bed far outweigh the potential risks of allowing the patient a fair degree of freedom

A single bed and firm mattress are preferable for nursing purposes. Careful bed-making contributes greatly to the patient's comfort. A rubber mackintosh across the bed covered by a taut drawsheet will prevent extensive soiling and save linen. The bed should be made twice daily—oftener if the patient is perspiring profusely. An adequate supply of pillows will make for comfort. Bedclothes should be light and not tucked in tightly a cage at the foot is often desirable. Quietness in the sickroom and its environment is essential. Traffic in and out of a sickroom should be cut down to a minimum.

The ideal sickroom should be bright and adequately ventilated and heated. Proximity to a bathroom, which should if possible be reserved for the patient's use, is advantageous. The temperature should be kept around 55° F. except in the case of infants or the aged, when it may be raised to between 60° and 65° F Even when the room temperature is low the patient can be kept warm by hot-water bottles—and this is particularly appreciated by the elderly.

Nursing.—Practically all of the common infectious diseases, provided the illness is not unusually severe or complicated, are best treated at home The mother will as a rule prove the best nurse. With modern therapy the period of heavy infectivity is comparatively short, so that the risk of spread of infection is slight The mother should be given instructions in simple home nursing and, in particular, emphasis should be placed on the following points.

An overall should be worn when attending to the patient and should be hung conveniently near the door. A bowl of chloroxylenol (Dettol), or even plain water, with soap and towels, should also be adjacent to the door and the mother should be instructed to use this frequently for hand-washing The practitioner should be careful to practise what he teaches. A simple temperature chart should be constructed, the thermometer should be placed in the groin or the axilla and left in position for two minutes. All treatment ordered should be entered on the chart and precise instructions given regarding administration.

The patient's *skin* should be kept clean by sponging with soap and warm water daily, especial care being paid to areas liable to soiling These should be freely dusted with talcum powder. The body should be washed and dried limb by limb. The windows, of course, must be kept closed during the bathing process. The refreshing and soothing effect of a " blanket bath " of this

nature is of inestimable value in any febrile condition Frequent massage of pressure areas with spirit must always be advised, the seriously ill patient must have his position changed every four to six hours.

Food should be given at strictly regular intervals and any food remains should be removed from the sickroom and burnt Cold water or other suitable fluids tastily flavoured must be given without stint and be offered at frequent intervals. In young children the *mouth* should be gently cleansed after each meal by inserting the index finger enveloped in cotton-wool soaked in warm water or warm solution of bicarbonate of soda containing 2 g. (30 gr.) to 570 ml. (1 pint) In older children the teeth should be brushed and the mouth rinsed with warm water or mild antiseptic solution The lips may be smeared with vaseline.

crusting and excoriation

The *eyes* may require regular cleansing, and saline swabbing is usually best. In adults care should be taken during long periods of toxæmia that the eyes are closed periodically. A drop of castor oil in the conjunctival sac morning and evening may prevent ulceration

All *excreta* should be removed from the sickroom and consigned to the closet as quickly as possible. Care must be taken to avoid contamination of water-closet seats Specimens required for the physician's inspection should be placed in covered fly-proof receptacles. Bed-linen, towels, etc., which may have been soiled with excreta should be left soaking in weak lysol solution overnight before being thoroughly washed with soap and water Swabs used for wiping away discharges from the mouth, nose, ears, eyes and other organs must be burnt.

Food should be protected from flies In summer, spraying of the sickroom with dicophane (DDT) will usually prove effective in eradicating flies altogether.

Diet.—The characteristic change in the metabolism of the fevered person is the greatly increased destruction of the nitrogen-containing tissues of the body. Instead of endeavouring to make good this loss by an increased nitrogen intake, it is a better policy to supply an abundance of "protein sparers" in the form of carbohydrates. Fevered patients strongly dislike fatty foods. On theoretical grounds a high caloric intake is indicated, but in practice, owing

milk daily usually
6 fl oz) should b
peptonized, treat
circumstances.
is a most valuabl
the form of sweetened lemon or orange juice drinks From 150 to 300 g (5 to 10 oz) of glucose can readily be administered in the twenty-four hours Jellies, clear soups, eggs and custards are useful additions to the diet, and varying

flavouring agents can add spice to an otherwise monotonous round. Because of their low nutritive value, high content of extractives and relative cost, the various commercial beef-juice preparations have little to commend them.

The free intake of water favours the elimination of waste-products. Hence the patient should be encouraged to drink cold or hot water freely between feeds. Including glucose lemonade, the water intake should amount to at least 4 pints in the twenty-four hours. The best indication of an adequate fluid intake is the excretion of 1.5 to 2 litres of urine daily.

Alcohol should not be administered as a routine except to alcoholics or elderly patients, to whom ½ fl. oz. of whisky diluted with twice its volume of water may be given at two to four-hourly intervals.

Relief of Symptoms.—Drugs should only be prescribed when there are definite indications for their use, and should be administered in draught or powder form, not in tablets. Unless otherwise stated, the doses prescribed in this section are for administration to adult patients.

Pyrexia.—A raised body temperature is in itself not harmful. The presence of fever is a natural reaction to infection and it should not be assumed that the restoration of a normal temperature by means of drugs is necessarily desirable. When the temperature exceeds 103° F., the skin of the whole body should be sponged with warm (98° F.), tepid (80° F.), or even cold water. Quite apart from any effect in reducing temperature, the application of tepid or cold water to the skin exerts an important reflex tonic effect on the nervous, respiratory and circulatory systems, and is very refreshing for the patient. This is particularly important at night, and a tepid sponge-down will often soothe a restless patient and be followed by a period of good sleep.

Headache and Malaise.—A combination of 0.6 g. (10 gr.) of acetyl-salicylic acid and 15 mg. (¼ gr.) of codeine administered at intervals of six hours usually gives relief. Should headache persist, phenacetin, caffeine and phenazone—0.2 g. (3 gr.) of each—may be prescribed in place of the above, the powder to be repeated every two hours for three or four doses. Diminution of intracranial pressure by lumbar puncture affords immediate relief in infections of the central nervous system. In the most intractable cases a hypodermic injection of 15 mg. (¼ gr.) of morphine will be necessary. When headache is severe, a quiet environment and the exclusion of bright light add to the comfort of the patient.

Insomnia and Delirium.—Restlessness and inability to sleep are characteristic symptoms in febrile cases and should always be taken seriously. Nursing technique should first be reviewed and everything done to make the patient comfortable. Where sleeplessness is due to worry or anxiety, a hot toddy followed by 1 g. (15 gr.) of chloral hydrate, well diluted, is frequently successful. The relief of headache may cure the insomnia. If pain is keeping the patient awake, 1 ml. (15 min.) of tincture of opium may be added to the chloral mixture; relief may only be obtained by the hypodermic injection of 10 to 15 mg. (⅙ to ¼ gr.) of morphine.

Paraldehyde, 8 ml. (2 fl. dr.), is another excellent and safe hypnotic; unfortunately it has a most unpleasant taste and odour. It may be administered by mouth well diluted with whisky or brandy and water, or by the rectum in double the oral dose. Cyclobarbitone, in a dose of 0.2 g. (3 gr.), and butobarbitone, 0.1 g. (1½ gr.), are valuable for their general sedative as well as their hypnotic effect.

Once a sleeping draught has been prescribed, it is essential to see that the desired result is attained This may necessitate repetition of half the initial dose at hourly intervals up to the limit of safety for the particular drug employed. Detailed written instructions regarding dosage should be given to the attendant.

Mild confusion can usually be controlled by chloral and tincture of opium, but active delirium calls for the hypodermic injection of 15 mg. ($\frac{1}{4}$ gr) of morphine with, in cases of maniacal excitement, the addition of 0 6 mg ($\frac{1}{100}$ gr.) of hyoscine hydrobromide; the injection may be repeated after an interval of one hour

Nausea and Vomiting.—Common initial symptoms in many febrile conditions, nausea and vomiting are rarely sufficiently severe or persistent to call for active treatment. In the majority of cases the symptoms will rapidly subside as soon as specific therapy brings the infection under control

When vomiting is persistent and severe, the electrolyte disturbance may require to be rectified by intravenous infusions This demands the closest co-operation between biochemist and clinician and is in general beyond the scope of domiciliary practice (see p 96).

Constipation.—In most infections constipation is present The only satisfactory method of emptying the bowel, and it is usually desirable to do so, is by the administration of a bowel wash-out. Soap and water or warm saline may be used and should be run in by means of a catheter and funnel. A Higginson's syringe should never be used. After the fluid has run in, if soap and water is used, the patient should be placed on a bed-pan, if saline has been used, the fluid contents may be syphoned off into a receiver at the side of the bed—usually better if the patient is extremely toxic. Either of these procedures is much less exhausting to the patient, and more sure in its action, than the administration of purgatives Should constipation be a feature of the illness, as for example in enteric fever, the bowel should be washed out every second day.

In convalescence from a severe fever the bowel habit has to be regained. [illegible] treatment

DISINFECTION

The aim of disinfection is to destroy the germs which are released from the patient in the various excretions Objects with which the patient comes into contact, particularly clothing and utensils, are liable to be contaminated with pathogenic organisms, and may remain a potential source of infection to others for a varying period of time

The daily disinfection carried out in the sickroom is termed "current" disinfection. The disinfection of the sickroom after removal of the patient to hospital, or after recovery, is termed "terminal" disinfection. The more efficiently "current" disinfection is performed the less need will there be for an elaborate disinfecting ritual after recovery.

Current Disinfection

The aim of current disinfection is to prevent the spread of bacteria from the patient to his surroundings. If steps are not taken to limit such spread,

[illegible]

observing some simple rules The hands will become grossly contaminated by bed-manipulations, cleansing of discharges, etc., and the importance of washing the hands after any attention to the patient must be emphasized An overall or gown must be put on as soon as the sickroom is entered and removed before leaving The fact that the air and dust of the room is charged with infection should be explained. Damp-dusting, wet-mopping of floor surrounds and the avoidance of " brush-and-pan " should be insisted on. Vacuum cleaners are an asset—but when they are used, it must be remembered that the contents of the bag are heavily infected and that it should therefore be emptied with care.

The attendant must in this way be " inoculated " with the concept that the patient is the centre of a series of concentric circles of infection : this is most dense at the inner circle, and the constant endeavour must be to prevent spread outwards. The air and dust of the room form the important means whereby the outer circles become contaminated, so that all steps to reduce dust and the careless circulation of air which disturbs dust will tend to limit spread. These measures are not only of importance in preventing the infection of others; the patient himself, especially if nursed alongside other patients, may acquire secondary complications from the implantation (particularly in the respiratory tract) of organisms acquired from infected dust.

The use of a mask by the attendant is as a rule undesirable If the attendant has a cold and the patient is under the age of a year, the use of a mask is worthwhile , for at this period of life a very ill infant may have its chances of recovery reduced by the acquisition of secondary infection In such circumstances the wearing of a mask is particularly desirable when the baby is being bottle-fed. To be effective, a mask must be of the thickness of at least six to eight layers of fine gauze. Several masks must be available and during use must not be touched with the hands, except for removal. They should be placed in antiseptic after use and boiled before reissue. The wearing of a mask is often thought to infer a special efficiency in preventing infection, but it is worth emphasizing that among careless or untrained attendants the mask may constitute more of a danger than a safeguard.

The Patient.—All discharges emanating from the patient must be assumed to be infective Attention should be particularly directed to :

The Respiratory [illegible]
use of gauze handke[illegible]
should be carefully [illegible]
in paper bags to be burnt

Alimentary Tract.—Vomitus should, if possible, be collected in a basin and immediately disposed of. The basin should be disinfected by wiping with weak lysol and washing in hot soapy water. If the linen is soiled, it should be steeped in disinfectant and then washed. Children who are ill often vomit unexpectedly, and the bed-linen may be saved by the use of towels and old sheets at the top of the bed or cot Fæces and fæces-soiled bed-linen must be promptly disinfected.

Discharges from Wounds, Abscesses, etc—Strict asepsis is of course essential in attending to wounds. Steps should be taken to avoid soiling of pillows and bed-linen with discharge, for as this dries it may be shaken off to form infected

dust. All fluids removed for testing (blood, cerebrospinal fluid) must be disposed of carefully.

Articles closely associated with the Patient.—The most important of these are the bedclothes, linen, towels, etc. All of them become heavily contaminated, and if the bed is made vigorously, organisms will be liberated into the air of the room The enclosing of the blankets in linen sheets will tend to limit the amount of fluff disseminated when beds are made The attendant should be instructed to avoid vigorous movements of bedclothes, mattresses,

in children Books and papers should be burnt, and most toys can be adequately disinfected with soap and water at the end of the illness

Terminal Disinfection

After recovery from the common infectious diseases, less importance is now attached to the terminal disinfection of the sickroom It is now realized that the patient is the real danger. Apart from tuberculosis there is little risk of infec-

treated in the manner already described The mattress, outer garments, carpets, etc , should be exposed to fresh air and sunlight for a day or two , carpets should be run over with a vacuum cleaner. The room and furniture should be washed with soap and warm water After thorough ventilation for twenty-four hours, the room may be regarded as fit for further occupancy.

Formalin Spray.—The elaborate disinfecting procedure necessary after the removal of a case of smallpox is carried out by the local Public Health Department and includes such measures as the steam disinfection of all bedding and clothing, and the spraying of the room with formalin, 8 fl oz to the gallon of water, followed by closure for six hours

In typhus fever, special measures have to be taken to destroy lice (see p 49)

The reader is referred to textbooks on Hygiene for details of these procedures

ANTHRAX

Anthrax is a gastro-intestinal infection which affects horses, cattle, sheep and goats The disease is conveyed to man through contact with infected

with animals or in wool, hair or hides. Infected shaving-brushes have in the past been responsible for the conveyance of anthrax infection in several instances.

Infection usually enters through minute wounds or abrasions on the exposed skin, giving rise after an incubation period of about twenty-four to thirty-six hours to a cutaneous lesion, the " malignant pustule ". The spores are occasionally ingested or inhaled, giving rise to the gastro-intestinal or pulmonary forms of the disease, which are almost invariably fatal within three to four days.

Anthrax is not a notifiable disease, but information regarding cases occurring in factories and workshops must be forwarded to the Chief Inspector of Factories at the Home Office.

Preventive Treatment.—Various legal enactments dealing with the disposal of anthrax-infected animal carcasses, the disinfection of infected cattle-sheds, etc., the disinfection of wool and hair imported from Asia and Egypt, and the prohibition of importation of Japanese shaving-brushes, have played an important part in diminishing the incidence of the disease in Great Britain. [illegible]

accommodation, etc. As a result, septicæmic anthrax is very rare.

So far as the individual is concerned, great care must be taken in handling infected material. Workers with skin lesions should be excluded. Where possible, protective gloves should be worn and are essential if there are any abrasions on the hands. Nurses or attendants must take all necessary precautions when handling infective discharges from the " pustule " or the respiratory and intestinal tracts Contaminated dressings should be promptly [illegible] mattresses and bed-linen must

[illegible] nthrax has undergone considerable change in recent years. In the past, early injection of Sclavo's anti-anthrax serum constituted the principal remedy. An initial intravenous injection of 100 to 200 ml of the serum was followed by daily intravenous or intramuscular doses of 100 ml, depending upon the severity of the case and the rapidity of local improvement Serum sickness almost invariably occurred from the use of such large doses of horse serum. The difficulty of supply in Great Britain has been overcome by setting up, in each Hospital Region a centre where serum is always available.

Penicillin alone, however, usually proves adequate for the majority of patients, but in cases of particular severity (e g infections of the neck) a single injection of serum will hasten the reduction of œdema. Since the need is to achieve a high concentration of penicillin in the region of the local pustule, large doses (200,000 to 500,000 units four-hourly) of the aqueous solution should be administered intramuscularly Treatment should be continued for a period of five to seven days, depending on the severity of the lesion. A local dressing of penicillin cream is a useful addition, since it reduces any chance of contamination of bed-linen, etc.

Treatment of the Lesion—As excellent results follow purely medical treatment, the local lesion should never be excised Immobilization of the affected area either by sandbags or splints is essential. In the most severe cases there may be extensive sloughing. *Skin grafting has been successfully carried out in* convalescence after excision of the slough.

CHICKENPOX

(Varicella)

A viral disease of high infectivity, chickenpox is probably spread by droplet infection and by conveyance of material from the skin lesions either on the hands or clothes of a third person, or possibly by air The incubation period is usually from thirteen to sixteen days It is rarely less than eleven days or more than twenty days. The disease is probably infective for at least twenty-four hours before the appearance of the rash The duration of infectivity is uncertain, but for practical purposes may be regarded as persisting until the last crust has separated from the skin.

Chickenpox is not a notifiable disease, but should smallpox be prevalent in a particular area, chickenpox cases may have to be reported to the local Public Health Authority.

Preventive Treatment.—There is no method of prophylaxis against chickenpox The regulations which are still applied by some school authorities in regard to quarantine require to be reviewed. There is much to be said for the cessation of attempts to avoid the acquisition of this mild infection in childhood. The disease in the adult can be more severe and can occur in most inconvenient circumstances. The association between chickenpox and herpes zoster should be remembered, for the latter disease quite commonly produces chickenpox in susceptible contacts and *vice versa*

Curative Treatment.—*General Management*—The treatment of chickenpox is on general lines, no specific remedy being available. Even in mild attacks it is wise to confine the patient to bed during the efflorescence of the eruption. When the rash is profuse, bed should be enforced until the lesions have crusted. If there is a tendency to scratch the pocks, the hands may be [illegible]

starch.

[illegible]

step must be to ascertain the type of the pathogen present and its antibiotic sensitivity. The administration of a suitable antibiotic for the streptococcal or staphylococcal case will suffice If *C. diphtheriæ* is the cause, serum must of course be given.

DIPHTHERIA

Diphtheria is almost entirely a toxic disease. Although some slight tissue invasion takes place in severe infections, for the most part the organisms remain localized to the site of inoculation from which the toxin diffuses by lymphatics and blood stream to all parts of the body. The ability of the host to neutralize toxin thus constitutes an almost complete defence ; for, shorn of its toxic action, the diphtheria bacillus is a weak pathogen.

C. diphtheriæ is divisible by cultural methods into three main types—*gravis*,

intermedius and *mitis*. Broadly speaking, the first two are associated with a more severe form of the disease. Bacteriological typing, however, is not of immediate importance to the clinician, who must estimate the initial dose of antitoxin before such information is available. The subsequent progress of the case, however, should be governed to some extent by the results of typing; *gravis* and *intermedius* infections should generally be allowed more careful and prolonged convalescence. Further, almost all *gravis* and *intermedius* strains are virulent, so that a carrier of these types may be regarded as harbouring pathogenic organisms *Mitis* strains are frequently non-virulent, and a virulence test is essential before the final assessment of a carrier can be made. The importance of typing in epidemiological work will be obvious

Cases and carriers constitute the main sources of infection. Usually the bacteria are carried in the throat or nose, the latter site being rather more common, so that in a search for a source of infection nasal cultures should never be omitted. Cutaneous diphtheria, often simulating a chronic sore, may be an unsuspected source of infection. Although in most instances infection is spread by droplet infection, contaminated milk, ice-cream and food have initiated local outbreaks.

Diphtheria is a notifiable disease It has an incubation period of two to five days

The importance of the early diagnosis of diphtheria cannot be too strongly emphasized Careful examination of the fauces should be a routine procedure in every febrile patient. Apart from the presence of "false membrane", marked faucial and palatal œdema, accompanied by an acute gross enlargement of the cervical glands, should, in a child, always be treated as diphtheria until proved otherwise.

Prevention and Epidemiological Control.—*Schick Test*—Susceptibility to diphtheria can be ascertained by the application of the Schick test—an intradermal injection into the left forearm of 0 2 ml of diluted diphtheria toxin Individuals showing an area of erythema from 1 to 4 cm. in diameter around the site of injection four to seven days after the application of the test are said to be Schick positive, an indication of susceptibility to the disease. When applying the primary Schick test to a large community, the highest proportion of positive results will be obtained when the reactions are read on the seventh day. No local reaction appears in those who are immune (Schick negative reactors). A precisely similar injection is made into the skin of the right forearm, but with toxin which has been previously inactivated by heat. This control test discriminates between local reactions arising from sensitization to the protein present in the test fluid and the true positive Schick reaction. Reliable Schick and control test material can be obtained commercially.

Active Immunization.—Every child should be actively immunized against diphtheria between the ages of eight and twelve months. A preliminary Schick test is unnecessary.

Various immunizing preparations, termed diphtheria prophylactics, are available commercially, of which the best are purified toxoid aluminium phosphate (PTAP), alum-precipitated toxoid (APT), formol toxoid (FT) and toxoid-antitoxin floccules (TAF). Two intramuscular injections each of 0 5 ml. of one of the alum-toxoids, administered at an interval of four weeks, will render at least 95 per cent. of children immune to diphtheria within six weeks of the second injection. Young children and infants show no reaction to these

doses, but in older children and adults it is preferable to reduce the initial dose to 0·2 ml.

The first injection merely acts as a "priming" stimulus and has no per- [illegible]

status of a person who has had a single injection of any of the diphtheria prophylactics. *Formol toxoid* is liable to be followed by unpleasant side-effects when injected into persons over eight years of age, but is an excellent prophylactic for infants and pre-school children *Toxoid-Antitoxin Floccules* has the advantage of being particularly free from unpleasant reactions and is therefore often used for children over the age of eight years. The content of horse serum is a slight disadvantage The course consists of three injections each of 1 ml. at intervals of two to four weeks For all of the prophylactics the injections should be made intramuscularly or by deep subcutaneous injection either into the deltoid or into the fleshy muscles below the spine of the scapula. (Combined immunization against whooping-cough and diphtheria is dealt with on p. 51.)

The diphtheria prophylactic antigens produced by the different manufacturers are of such standard potency that it is unnecessary to carry out Schick tests after immunization Although absolute protection against diphtheria cannot be guaranteed in every individual who has completed the immunizing course, marked modification in the severity of a subsequent attack is to be expected. The duration of immunity varies, but in all except a small percentage of children lasts for some years The important consideration is that the child has been trained in antitoxin production so that a small dose of antigen subsequently will evoke a sharp rise in antitoxin. The next period of danger in the child's life is when entering school, *so that a single intramuscular injection of 0·2 ml. diphtheria toxoid when the child commences his school career should be re-* [illegible]

procedures must not be carried out during the summer months.

General Measures—For the control of an outbreak the first steps are the isolation of the case and the disinfection of all articles likely to be contaminated with the faucial or nasal secretions of the sick person. Household or institutional contacts must be carefully examined for evidence of a missed infection. Any person suffering from chronic nasal or aural discharge, or obviously unhealthy tonsils—or a suspicious cutaneous lesion—should be isolated, and swabs taken from nose, throat or other suspicious site

Indiscriminate swab-taking from all contacts as a measure of control should in general be avoided, for "positive" reports on microscopic examination at twenty-four hours may be misleading and typing will usually take three or four days to complete. When a single case is discovered in a closed community, a careful examination of the contacts should be made and those with an unhealthy condition of the nose, throat or ear selected for immediate bacteriological examination. *All contacts should be examined daily for seven days*, and on the slightest suspicion of clinical infection, antitoxin in adequate dosage should be administered. Knowledge of the type of organism in the primary case is of

dangerous.

In the unusual event of an outbreak in a community whose members have not been previously immunized, combined active-passive immunization should be practised. To accomplish this, 500 units of antitoxin should be injected into one arm at the same time as an injection of 0 5 ml. of alum-precipitated toxoid is injected into the other arm The course is completed by giving a second injection of toxoid one month later. When all the members of the community are known to have received in the past a full immunizing course of injections, a single injection of 0 2 ml. of a diphtheria toxoid will rapidly achieve a useful state of immunity.

It must be emphasized that a history of immunization should not lead the practitioner to ignore the possibility of diphtheria. Indeed, it must be

It is even more necessary than ever for the practitioner to acquire the habit of injecting from 4,000 to 8,000 units of serum when, in a suspicious case, a history of contact or the appearance of the throat suggests the necessity of a swab examination. It is not sufficiently realized that 4,000 units of refined diphtheria antitoxin is contained in a bulk of only 1 0 ml. and that the chance of development of serum reactions with this product is small. Finally, it should be noted that the infectious diseases hospital is always prepared to receive cases for " observation ".

Curative Treatment.—The four essentials in the treatment of a case of diphtheria are: (1) early adequate serum administration; (2) absolute rest in bed for a varying period of time according to the severity of the disease; (3) skilled nursing, and (4) the free administration of glucose.

Antitoxic Serum—An intramuscular injection of at least 4,000 units of

this might be diphtheria " is under an obligation to give serum at once Swabs can then be taken. By the time full bacteriological investigations have been made, several days must elapse. These are the critical days: omission of antitoxin treatment at this stage may be fatal. There is considerable difference of opinion regarding the optimum dose of antitoxin in the treatment of diphtheria. Broadly speaking, mild attacks require from 4,000 to 8,000 units intramuscularly, cases of moderate severity from 16,000 to 32,000 units intramuscularly; severe or toxic attacks from 64,000 to 96,000 units of antitoxin both intramuscularly and intravenously. When the diphtheritic infection is limited to the larynx, 8,000 units of antitoxin are usually sufficient, and in purely nasal diphtheria, unless toxæmia is severe, a similar dose is adequate.

In endeavouring to assess the *amount* of serum required, three clinical estimates may be combined:

(i) Although no amount will compensate for delayed administration, a patient seen late should receive a large dose of antitoxin.

(ii) In general, the more membrane the more toxin formation, and therefore the greater need for a large dose of antitoxin. In particular, large doses should always be given when the membrane extends to the uvula, nasopharynx or soft palate. (It should be remembered that severe gravis infections often show a small amount of true membrane but tremendous œdema and "glairiness" of the soft palate, simulating quinsy Such cases should always receive a large dose.)

(iii) Extensive enlargement of the tonsillar glands calls for a large dose of serum.

There is no satisfactory method of assessing the correct amount of antitoxin, so that it is better to err on the side of overdosage. There are good grounds for believing that a dose of 48,000 units is more than adequate for the most severe case of diphtheria and that it should never be necessary to give more than 96,000 units

The *route of administration* is very important. It is rarely appreciated that a considerable time elapses after intramuscular injection before "peak" levels are attained in the blood stream *All severe cases* (i.e. *where more than* 32,000 *units are to be given*) *must receive at least part of the dose intravenously*. In other words, the intramuscular route is the second-best route and should only be used [illegible]

Other Specific Treatment.—The bacteriological examination of the throat [illegible]

[illegible] and secondly it hastens the disappearance of C *diphtheriæ* from the throat and reduces the risk of development of the carrier state The dose must be large [illegible]

Glucose—Glucose lemonade should be freely administered and an intake by mouth of 150 to 300 g (5 to 10 oz) of glucose daily is desirable; 500 ml. of a 5 per cent. solution of glucose saline may be given with the dose of intravenous antitoxin. Large intravenous infusions are, however, to be avoided in severe infections, and it is therefore preferable to give 50 to 100 ml of a 25 per cent glucose solution, repeated, if necessary, at eight-hourly intervals.

General Measures—With the exception of the mildest attack, a case of [illegible]

penicillin should never be the antibiotic of first choice. Treatment should be started with a tetracycline while sensitivity tests are awaited ; after more precise information is available, the suitable antibiotic can be chosen. Even after tracheotomy such cases often pursue a stormy course and require constant expert supervision.

BACILLARY DYSENTERY

Dysentery must now be regarded as an endemic infection in large cities. In all parts of Great Britain notifications of the disease have increased greatly in recent years, and in view of the mild nature of the symptoms it may be assumed that the notifications represent but a proportion of the actual incidence. It is no longer true to say that the maximal incidence is always in the summer months. Notifications have been excessive throughout the year, and, in some years the peak has occurred in the first quarter. A large proportion of the infections is in children under five years of age. It is not sufficiently well known that the presence of blood or mucus is not a necessary feature of the illness, and in many cases a few loose stools may comprise the whole complaint. As a result, many infections are missed and so increase the spread of the disease. Some convalescents become temporary carriers and act as a source of infection.

Dysentery is seldom a[illegible]
in a family it is usual to [illegible]
stools Outbreaks in day [illegible]
and here again the diagnosis of one case will often unmask a widespread epidemic of carriers.

In Great Britain Flexner and Sonne types of *Sh. dysenteriæ* account for the great bulk of infections.

Unlike typhoid fever, which is of course spread in a similar way, the infection remains almost entirely localized to the bowel and agglutinins do not appear in the blood to any great degree Apart from toxic absorption due to bowel ulceration, the main danger in severe infections arises from exhaustion of the patient by loss of fluid and salt in watery stools. This results in dehydration and hypochloræmia, the degree of which is dependent upon the character of the stools and the duration of diarrhœa. Such a degree of severity is fortunately unusual.

Diagnosis depends on accurate bacteriological examination. For this purpose a rectal swab outfit is to be preferred since the specimen can be secured quickly and easily. No time should be lost between obtaining the specimen and submitting it to the laboratory The use of the rectal swab combined with improvement in selective media has added great precision to the diagnosis.

Dysentery is a notifiable disease.

Prevention and Epidemiological Control.—The control of ward and institutional outbreaks often presents an overwhelming task. All further [illegible]

and he should therefore be forewarned Plans should also be prepared for the separation of those found to give positive results and arrangements made for the sterilization of food utensils, bed-pans, etc. Soiled napkins should be dropped direct into pails containing chloroxylenol (Dettol). The nursing staff must be instructed regarding the method of transference of the infection and

loose or green stool should be reported at once.

The extent to which bacteriological freedom from infection prior to dismissal is enforced must vary from case to case. When the patient is to return to a closed community—service personnel and children from nurseries—and when there is close association with food preparation it is desirable to obtain at least three negative bacteriological reports. When the patient is returning home, however, it is unnecessary to carry out protracted examinations, and the average case may be regarded as free from infection by the eighth to tenth day of illness

Curative Treatment.—The majority of cases, due to Sonne and Flexner infections, run a mild course of three or four days and call for little medicinal treatment. The administration of specific serum to cases of Shiga infection is of undoubted value. The dose is up to 100 ml. and the injection should be given intravenously.

Sulphonamides.—In most parts of Great Britain the endemic strains of shigella have now acquired resistance to sulphonamides, which are therefore no longer effective. In areas where this is not the case, sulphadiazine will prove as satisfactory as sulphaguanidine or succinylsulphathiazole.

Antibiotics—It seems at first sight rather excessive to suggest the use of a tetracycline as a treatment for such a mild disease. It is undoubtedly effective in securing bacteriological clearance and does so in low dosage (60 mg./Kg / day) This is undoubtedly important in dealing with food-handlers, etc. It should be used with caution in hospital wards, where the danger of superinfection of the bowel with resistant staphylococci is very real It is doubtful if this complication will be encountered in general practice. The period of treatment should not exceed five days

General Management.—The patient must be confined to bed and kept warm from the first symptom of the disease. When the attack is severe the bed-pan should be employed in order to avoid contamination of lavatory seats, etc. When the call to stool is incessant, the bed-pan may be dispensed with and the motions received into tow, which, when soiled, is collected and burnt.

Provided the diet prescribed is nutritious, easily assimilable and with little

gradually to the diet These dietetic restrictions are necessary in severe cases, but it must be appreciated that the common endemic disease is so mild that the patient is able to take ordinary food.

Carriers.—Persistent symptomless carriers are sometimes unmasked in the investigation of an outbreak. For such cases tetracycline, oral streptomycin, streptomycin combined with sulphonamide or polymyxin B may prove effective. Such cases should not be kept in hospital for prolonged periods unless in strict isolation. In the open ward with other dysentery patients they will be subjected to constant reinfection.

THE ENTERIC FEVERS

(*Typhoid and Paratyphoid Fevers*)

The annual occurrence in Great Britain of one or more outbreaks of enteric fever indicates that, in spite of sanitary precautions, the risk of contamination of water and food supplies with the enteric group of organisms still persists. *S. typhi* and *S. paratyphi B.*, the organisms commonly met with in the British Isles, are excreted in the stools and urine during the course of the illness. The unsuspected ambulant case, the missed case, the temporary carrier and the chronic carrier play a very important part in the dissemination of enteric fever. It is probable that even with efficient chemotherapy from 2 to 5 per cent. of all cases of typhoid fever become permanent carriers. That the incidence of the chronic carrier state is higher in women than in men is unfortunate when we consider the possibilities of contamination of food in course of preparation. Although the fæcal carrier is more commonly encountered, the urinary carrier is potentially more dangerous. The organisms are discharged intermittently in both stools and urine, so that repeated bacteriological examinations are essential before the carrier state can be excluded.

Although isolation of the pathogen from fæcal and urinary specimens is th only exact method of diagnosing carriers, preliminary examination of the bloo serum may serve as a useful "screening" test when large numbers of suspects have to be reviewed. Antibodies for the Vi antigen are almost always to be found in fairly high titre in carriers, so that if a preliminary blood test is carried out, attention can be directed particularly to those with such antibodies.

Outbreaks, then, are usually a result of the contamination of food or water by a missed case or carrier. Milk or milk products, prepared meats, uncooked vegetables, fruit and shellfish constitute the usual vehicles of infection. A nurse may contract the disease in the course of her duties; this usually indicates carelessness in the washing of hands. It is important to make a specific prohibition of the eating of any food by the attendant in the ward or room where the disease is being nursed.

The incubation period of typhoid infections is from twelve to fourteen days, and of paratyphoid B from ten to twelve days.

Typhoid and paratyphoid fevers are notifiable diseases.

Prevention and Epidemiological Control.—The control of typhoid fever is essentially a problem for the local Public Health Authority and embraces such factors as an efficient system of sewage disposal, a safe water and milk supply, the detection of carriers, the supervision of shellfish, the control of the house-fly and protection of food against contamination by rats and mice.

Careful supervision of sewage and water is a commonplace in the large towns, so that widespread epidemics of typhoid are now unusual. In country districts, however, defective cesspools, flooding or ineffective disposal of sewage are still commonly the source of localized outbreaks. Milk, and particularly ice-cream, is now replacing water as the vehicle of infection, especially of paratyphoid fever, and here the towns are in as much danger as the countryside; but although day-to-day control by Public Health Departments forms an important part of the protection of the public, the early diagnosis of the infected case by the practitioner is of prime importance both in stemming an incipient epidemic and in stopping it once it has started. The value of early blood culture in cases of continued fever must here be emphasized; and the

should be inoculated. It is now generally agreed that "provocation typhoid" is a negligible risk and that in such circumstances immunization should be undertaken.

recommended is 1 to 2 g. daily for a period of five days. Longer periods of treatment have been advised with a view to eliminating relapse but have not in fact been very successful It seems more logical to give a short course and to be prepared to repeat treatment if relapse occurs. A high initial dose is both unnecessary and unwise, since a "Herxheimer" effect has been noted in some severely ill patients. Chloramphenicol treatment often produces remarkable improvement within twenty-four to forty-eight hours, especially when begun early, but it should be remembered when treatment is started late that in spite of the patient's well-being the ulceration of the bowel and muscular degeneration resulting from toxæmia are still present It is therefore essential to maintain complete bed rest for a period of two to three weeks, until healing of the ulcerated bowel has occurred. Relapse is still a prominent feature of the disease, but fortunately responds to a second course of chloramphenicol.

General Management.—A practitioner who undertakes the treatment of a case of enteric fever in the patient's home must not only satisfy himself and the

recovery is secured. Hospital is the ideal place for treatment, and it is very important that the patient should be removed there at an early stage of the illness

The patient must be kept strictly recumbent, but his position should be altered several times daily. Mental rest is essential, and visitors must be excluded. A four-hourly chart must be kept and arrangements made for the prompt notification of serious symptoms to the physician Stools, urine and other discharges, wash water, soiled linen, nursing utensils, etc., require to be carefully disinfected, and the patient's crockery, cutlery, etc , must be boiled after use Measures should be taken to rid the sickroom of flies The nurse must on no account prepare or handle food which is to be consumed by other members of the household

The mouth and skin require regular and careful cleansing, and precautions have to be taken to prevent the development of pressure sores.

Retention of urine is liable to occur and should receive appropriate treatment. Inspection of the stools, abdomen, lung bases and heart should form part of the physician's daily routine examination

Diet.—Although treatment with chloramphenicol will often produce rapid amelioration, it must be emphasized that, if bowel ulceration has occurred, time for healing must be allowed. The duration of a strict dietetic régime is now greatly shortened; but it is essential in the early days of treatment to enforce a low residue diet and to be sure that all evidence of intestinal inflammation has

2,000 calories may be attained. During the early days of the illness a fluid diet should be administered. The use of a "composite" food such as Complan (Glaxo)—even if only for a part of the diet—makes it easy to ensure that the intake is adequate. Towards the end of the first week, in addition to 2 pints of milk daily, such readily digestible articles as lightly boiled eggs, custard, ...

time and each feed should be consumed within fifteen minutes Feeds should be given at two-hourly intervals, between 7 a.m and 9 p m and twice during the night when the patient is awake.

Plain cold water or fresh orange, lemon or grapefruit drinks sweetened with lactose or glucose should be administered at least every half-hour between feeds. A daily fluid intake, apart from meals, of at least 2 litres (4 pints) is desirable.

Complications.—As soon as the patient has been effectively brought under chemotherapeutic control, the symptoms and signs which were formerly dreaded—persistent diarrhœa, meteorism and intense toxæmia—rapidly disappear. Only two points need to be borne in mind, first, ulceration may still ...

and ...

look

the illness On the first appearance of blood in the stools ...

extra hot bottles provided and blood transfusions administered. Preparations such as hæmoplastin or coagulen-ciba are of no value and are no substitute for transfusion.

Nothing should be given by mouth, except water and fragments of ice to suck, until the hæmorrhage has ceased ... hourly administration of 7 ml. (2 fl. dr) ... the amount to be cautiously increased ... adequate. Aerated waters are best avoided

If the bowels have not moved, an olive-oil enema may be given four days after the hæmorrhage has ceased ...

Phlebitis—Thrombosis in the veins of the lower limbs is a common complication during convalescence. The affected limb is immobilized with pillows for four weeks, after which period gentle massage and passive movements may

be started. Suitable analgesics will help to relieve the early pain. The use of anticoagulants is contra-indicated because of the danger of precipitating hæmorrhage from the bowel.

Other Complications.—The pain of cholecystitis can be relieved by the local application of hot fomentations and the hypodermic injection of morphine and atropine.

Periostitis or osteomyelitis must be treated on surgical lines. Material from a periosteal abscess may contain typhoid bacilli, and soiled dressings should be handled with care.

Convalescence.—It is advisable to confine the patient to bed for at least fourteen days after the temperature has returned to normal. By this time the danger of relapse is usually past Three consecutive negative cultures for

often superimposes itself upon some pre-existing chronic condition. Here again, *the treatment of the established carrier is still far from satisfactory.* Adequate chloramphenicol treatment during the acute stage reduces, but

ith many chronic carriers,

the disease. In the case

ry tract is desirable, for it

is sometimes possible to rectify a coexistent abnormality. The fæcal carrier state is often associated with chronic cholecystitis; modern methods of anæsthesia have so greatly reduced the hazards of surgical interference that cholecystectomy should receive serious consideration in such cases. When the carrier state is found to arise from a chronic bone lesion, appropriate surgical measures are usually successful.

In some cases a combination of sulphathiazole and penicillin has proved effective. Sulphathiazole is administered orally—for an adult 2 g. four-hourly for seven days. Penicillin is administered systemically at the same time, 15,000,000 units being administered over a period of seven to ten days.

at three-day intervals of three doses each of 4 g. of soluble iodophthalein as used in the X-ray examination of the gall-bladder has occasionally been successful in

been excreting typhoid bacilli for more than one year Just as important, no

Members of the household to which the carrier returns should be inoculated against enteric fever.

ENCEPHALITIS LETHARGICA

(Epidemic Encephalitis)

(See p. 808)

ERYSIPELAS

Curative Treatment.—*Sulphonamides*—The use of the sulphonamide group of drugs has so greatly hastened recovery that no other form of treatment

adult 6 g daily should be administered for a period of seven days; under the age of five years a daily dose of 3 g will be found satisfactory. Children tolerate the drug exceedingly well, and, as the disease is more severe in infancy, relatively large doses may be employed

Penicillin.—Penicillin also achieves rapid cure in erysipelas, but in view of the excellent results obtained with the sulphonamides and the ease of their administration, it is not the treatment of first choice Exceptions to this general rule are: erysipelas of the leg, in which there is a tendency for invasion of the cellular space with abscess formation; lesions associated with massive œdema, and if attacks recur. In such cases the intramuscular injection of 200,000 units four-hourly for a period of five days will give more satisfactory results.

Local Treatment.—No type of local treatment has any beneficial effect upon the dermatitis. Local applications may be used to relieve pain and œdema. Compresses of carbolic lotion 1 · 60 or 1 : 80, anhydrous magnesium

treatment. Should the glands suppurate, incision should be delayed until complete coalescence has occurred and fluctuation is demonstrable. Healing is then more rapid Subcutaneous abscesses are not infrequent. Here, again, incision should not be made too early.

GLANDULAR FEVER

(Infectious Mononucleosis)

Epidemics of this acute infectious disease of virus ætiology occur in schools and institutions, and sporadic cases are common among the general population.

Although susceptibility to the disease appears to be almost universal, the degree of infectivity is not high. For example, cases of glandular fever can be treated in a mixed ward with no ill results. The incubation period is usually between five and fifteen days. Fever accompanied by acute enlargement of the lymph glands, particularly of the neck, is the form of the disease commonly met with *in children Febrile and anginose types occur in young adults. A mononuclear* leucocytosis is characteristic of the disease. The Paul-Bunnell sheep-cell agglutination test has proved a valuable aid to diagnosis; agglutination in a titre of 1 . 160 or higher may be regarded as diagnostic. The bacteriologist should be informed if horse serum has been administered, since this causes false positive results.

Glandular fever or infectious mononucleosis is not a notifiable disease.

Preventive Treatment.—There is no specific method of prophylaxis against glandular fever

Curative Treatment.—There is no specific treatment: management of the disease is on symptomatic lines. The antibiotics have some value in the anginose forms of infection because of their effect upon the secondarily infecting organisms. Systemic administration is advisable; a period of three to four days' treatment will usually suffice

General Management.—The patient should be confined to bed until the temperature has been normal for one week and the glandular swelling markedly diminished. The febrile type with high and prolonged pyrexia, lasting several weeks, requires to be treated on the same lines as a case of enteric fever

Meningitis, epistaxis, hæmaturia and conjunctivitis are occasional complications.

Convalescence.—Recrudescences are liable to occur. Even after mild attacks anæmia and slight debility often persist for several months and the patient should return gradually to normal life. When convalescence is unduly prolonged, careful hæmatological examination is desirable, for some cases of reticulosis have an onset similar to infectious mononucleosis.

INFLUENZA AND VIRUS INFECTIONS OF THE UPPER RESPIRATORY TRACT

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recognized by virological techniques comprise at least one common cold virus, three types of influenza virus (A, B and C), the Sendai virus, the Coxsackie viruses and members of the group termed adenoviruses. It is now possible, though scarcely practicable, to make an accurate diagnosis of these infections either by growth of the virus from nasal or pharyngeal secretions, or by the demonstration of a rising level of antibody during the course of the illness. In some cases, indeed, both tests must be performed, for the mere demonstration of th

The pharyngitis,
exudativ ical form of
pneumonia. The less-virulent viruses cause only slight damage to the mucous membranes and the resulting illness is merely inconvenient; with others—

particularly the influenza viruses—cellular damage is more extensive, pulmonary involvement is a greater risk, and secondary bacterial invasion may produce serious illness The sharp rise in the frequency of pneumonia which occurs every winter is almost certainly related to an increase in the prevalence of one of the influenza viruses, and indeed, it seems probable that all pneumonias have their origin in a respiratory virus infection

The incubation period of all these infections is short—one to two days. Influenza is only notifiable when it is complicated by pneumonia

Prevention and Epidemiological Control.—There is no method whereby the spread of infection can be prevented Free ventilation and avoidance of crowds are clearly advisable, but since many people suffering from minor degrees of illness continue with their daily work, the prevalent virus is constantly present in crowded trains, trams and buses, and the avoidance of contact is virtually impossible

Prevention of influenza by the use of specific vaccines has now been extensively investigated, but although encouraging, the results are not yet sufficiently convincing to justify their general use. Two types of vaccine have been evolved The first is a formolized suspension of virus particles; the second contains an oil adjuvant which by delaying absorption enhances the antigenic effect. Both require two intramuscular injections of 1 0 ml, which are separated by a period of four weeks Unfortunately the resulting immunity is not of long duration and good results have been obtained only when the vaccine has been administered just prior to the occurrence of an epidemic.

The so-called "common cold vaccines" which are, of course, bacterial vaccines, have not the slightest effect upon the incidence of upper respiratory tract infection. Nor is there any evidence that mixed vaccines of the common secondary invaders have any effect in reducing the complication rate of influenza.

Curative Treatment.—*General Management.*—Ideally any person with an upper respiratory tract infection should be isolated from the community in bed until the temperature has returned to normal. Unfortunately, mankind is not so tractable, and the ability to "carry on" is regarded as a virtue There is no specific serum or drug treatment of proven value, so that the mainstay is efficient nursing and treatment of symptoms (see General Management of Fevers, p 1). The nursing procedures that require emphasis are the hygiene of the mouth, nose, eyes and skin For the relief of pain, aspirin and Dover's powder will usually suffice; when there is complaint of sore throat, the aspirin should be slowly [illegible]
has a local analges[illegible]
[illegible]

In the mild case, such a method of prophylaxis is not advised Pneumonia will often be suspected rather than accurately diagnosed, for the physical signs in the chest are seldom typical of consolidation. The response of influenzal pneumonias to chemotherapy is less dramatic than that of the pneumococcal variety, but penicillin in high dosage should be started at once on the appearance of suspicious symptoms *Staph. aureus* is the most frequent secondary invader and in many cases proves to be penicillin resistant If there is any delay in response to penicillin, therefore, erythromycin or a combination of penicillin

with streptomycin should be given. With streptococcal or staphylococcal [illegible]

suspected, there should be no delay in starting chemotherapy. Delay and indecision on the part of the doctor may cost the patient his life.

Other Complications.—Pyogenic complications may arise in the para-nasal sinuses or middle ear. In this event there is less urgency in beginning [illegible] nsitivity testing [illegible] The antibiotic [illegible] iyocarditis must always be borne in mind, especially in the older patient

Convalescence.—The importance of an adequate period of convalescence after influenza must be impressed upon the patient. Owing to the toxic effect of influenza on the myocardium it is wise even in the mildest case to advise rest in bed for at least three days after the temperature has settled This applies particularly to those over the age of thirty-five years. In more severe attacks this period should be extended to one to two weeks. The response of the heart to increased exertion must be carefully watched, and a further rest enforced if this be unsatisfactory. Cough due to tracheitis is sometimes very persistent, but is usually relieved to some extent by the administration of a teaspoonful thrice daily of either elixir of methadone or syrup of codeine. Infected nasal sinuses may be the exciting factor and should receive appropriate treatment.

MEASLES

(Morbilli)

[illegible]

susceptibility to measles appears to be practically universal. The incubation period is usually from nine to eleven days, but may vary from seven to fourteen days.

In certain areas the first case of measles occurring in a household has to be notified to the Medical Officer of Health. Otherwise the disease is not notifiable.

Preventive Treatment.—*Passive Immunization*.—An attack of measles can be prevented or modified by the intramuscular injection of an appropriate dose of human convalescent serum or gamma-globulin in the early stages of incubation. Gamma-globulin is now generally available and is safer and more effective than convalescent serum.

Except in an ailing or weakly child, or in a child under two years of age, the aim should be to attenuate rather than to prevent an attack of measles. Such a procedure may enable the child to gain a lasting immunity. In hospitals, sanatoria or orphanages it is advisable to attempt complete protection as soon after exposure as possible.

The dose of gamma-globulin suitable for a child under five years of age is

set out in the following table. Owing to variations in the antibody content of human serum, complete protection cannot, however, always be guaranteed to follow the administration of the dosage indicated.

DOSAGE OF GAMMA-GLOBULIN IN MEASLES

Preparation	*Age (years)*	*Dose for Prevention*	*Dose for Attenuation*	*Time of Administration*
Gamma-globulin .	–2	675 mg.	150–300 mg.	1st–3rd day of incubation period.
	2–5	900 mg.		

[illegible] d,

[illegible] m

measles are usually excluded from school for three weeks from the date of onset of the last case in the house No restrictions need be applied to children who have previously suffered from measles. When measles is prevalent, susceptible children should not attend parties, the cinema or other gatherings

Measles is now a very mild infection Even when it assumes a severer form, the severity is due to bacterial invasion which can be promptly countered by the use of antibiotics. Children under the age of two years should never be needlessly exposed, but, since the acquisition of immunity may be regarded as part of the process of growing up, it is unwise indefinitely to postpone the infection. Accordingly no attempt should be made to avoid measles once the child is over two years.

Curative Treatment.—*General Management* —Immediately measles is suspected, the child must be isolated and confined to bed in a freely ventilated yet warm (60° to 65° F.) room Isolation not only prevents further spread but protects the patient, for the real danger of measles lies in the complications arising from invasion with such organisms as *Str. pyogenes*, the pneumococcus and *H. influenzæ*, so that contact with adults and strangers should be avoided. Although in some cases the patient may be harbouring these organisms in the [illegible]

Visitors should be discouraged until convalescence is established

Discharges from the mouth, nose and eyes should be collected on rags or paper handkerchiefs and promptly burnt

[illegible]

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and

sponged with soap and warm water once daily. Cream of magnesia or other mild aperient may be [illegible]

be paid to the hygie[illegible]

there by virus may c[illegible]

most irritating symptom is the persistent harsh cough. Inhalations of steam with Friar's balsam often relieve this and they are particularly effective for children; in adults syrup of codeine, by depressing the cough reflex, is the better treatment. If this fails to give relief, methadone may be tried.

Complications.—*Sulphonamide Prophylaxis*.—The danger of secondary bacterial invasion in measles is of short duration, for once the mucous membranes are healed, the risk diminishes. Provided the patient is being properly isolated and access of visitors prevented, there is no need for specific prophylaxis; but where several children are nursed together the danger of cross-infection from one to the other is increased and chemoprophylaxis is worth employing. Sulphadiazine should be used in therapeutic dosage until the rash has faded or for forty-eight hours after the subsidence of the fever. When *otitis media* occurs, bacteriological examination of the pus is very desirable. Penicillin, [illegible] rganism is sensitive to it; [illegible] of the infective organisms [illegible]

Broncho-pneumonia.—Broncho-pneumonia is the most serious complication. In most cases the organism is responsive to sulphadiazine, but penicillin may be used in severe cases.

A mild degree of *laryngitis* is a common early symptom in measles. As a general rule laryngitis during the catarrhal stage is of virus origin and improves as the rash appears. Laryngitis arising *after* the appearance of the rash is always more serious, and the possibility of diphtheritic infection should be kept in mind. If the child has not been immunized, a dose of 4,000 units of diphtheria antitoxin is desirable. Further treatment should be on the lines detailed on p. 652.

In the same way, gastro-enteritis may be expected during the catarrhal or early rash stage as a natural part of the disease; its occurrence, thereafter, should raise the immediate suspicion of dysentery.

The appearance of corneal ulceration calls for dilatation of the pupil, either by atropine drops or ointment (½ per cent.) and the use of 10 per cent. mild silver protein (B P.) drops thrice daily No time should be lost in obtaining the advice of an ophthalmologist.

Convalescence.—In an uncomplicated case the child may be allowed out of bed about the fifth to seventh day from the onset of the disease, and out of isolation on the tenth day.

MENINGOCOCCAL INFECTION [1]

It is now clear that acute meningeal involvement must be regarded as only one form of meningococcal infection. Two other syndromes—acute fulminating septicæmia often with adrenal hæmorrhage and chronic septicæmia usually unaccompanied by meningitis—are likely to be seen during epidemic periods; indeed, the practitioner should have them especially in mind during the first two months of the year when the annual prevalence is at its height. For the recognition of both, the first essential is that the clinician remembers the possibility of their occurrence; the features are sufficiently definite to permit a

[1] Since January 1950 all manifestations of infection by the meningococcus in Great Britain are notifiable under the general title " meningococcal infections ".

clinical diagnosis with a fair degree of accuracy. The attention of the practitioner is drawn to their existence, for in one—chronic septicæmia—correct treatment achieves rapid cure and may, in some cases, prevent subsequent meningitis; while, in the other, only the most rapid diagnosis and immediate institution of proper measures hold out any possibility of recovery. The whole course from

must thus be aimed not solely at the meninges but also at a systemic infection It is perhaps because the sulphonamides can follow so closely the route of the meningococcus that they have proved more efficacious than penicillin.

Meningococcal infections are notifiable

Prevention and Epidemiological Control.—There is little doubt that carriers play an important part in the spread of the disease, and because of this it used to be regarded as valuable to search for carriers on the occurrence of a case. It is now appreciated that a simple routine examination of the nasopharynx on a single occasion may well fail to isolate the organism, although repeated examinations will often succeed Indeed, in some carefully conducted studies it has been shown that practically all of the contacts were carrying the organism. This is especially the case in closed or semi-closed communities. Search for carriers has therefore been abandoned as a method of control. Fortunately, in the general population, case-to-case infection is not common and

dust by movement than to the actual close proximity of the inhabitants Good ventilation is thus of great importance. It is possible that minor upper respiratory tract infections assist in the spread of meningococci, and in army camps, after a case has occurred, patients suffering from such complaints should be closely examined—especially if there is fever or a complaint of headache

Sulphonamide prophylaxis was extensively practised, especially in America, during the 1939-45 war, not always with happy results. Sulphadiazine in doses of 1 g daily was given, and shortly after the onset of such treatment the carrier rate was greatly reduced; but when the drug was stopped, organisms reappeared in the throat with great rapidity—in some cases with a developed resistance to sulphonamides. This method of prevention, therefore, cannot be advised for widespread use. In army camps it has a place, but it is preferable to give the ... nple with sulphonamide

... well to remember that ... under five years. The practitioner should take every opportunity to reinforce the advice given at these times by the Medical Officer of Health through the press Crowded places

tion is better than sulphonamide alone. In infants, too, one is sometimes in doubt as to the amount of sulphonamide actually absorbed by mouth. Systemic penicillin ensures effective chemotherapy in a vomiting child.

(3) If there is a profuse eruption, coma or severe vomiting, penicillin parenterally and intrathecally should be given. The lessened toxicity compared with sulphonamide may be of value in such cases during the preliminary period of treatment.

(4) If blockage at the base of the brain is suspected, intrathecal penicillin at levels higher than the lumbar route should be used. Cisternal and even intraventricular injection is sometimes of help in refractory cases.

(5) If organisms are still present in the forty-eight-hour fluid or if relapse occurs, the administration of penicillin intrathecally may hasten cure. Occasionally individuals are encountered who are known to have been sensitized to sulphonamides, and such patients have been successfully treated with penicillin.

It needs to be stressed that the exceptions—when penicillin should be used—are far outnumbered by the occasions when sulphonamide alone is successful.

Retention of urine still remains a common occurrence which should always be looked for, and, when present, relieved by catheterization. For the relief of headache, repeated doses of acetyl-salicylic acid will often be found effective. Chloral hydrate is a useful sedative. Morphine is best avoided. Intense headache may often be relieved by lumbar puncture, but if a large amount of fluid is withdrawn it is probably wise either to increase the oral dose of sulphonamide temporarily or to give an intravenous injection of the drug.

Complications.—Broncho-pneumonia is the complication most to be feared. Although the pneumonia may be due to the *meningococcus* in some cases, cross-infection is the likeliest cause, masking of the attendants, the exclusion of adult visitors, and abundant fresh air for the patient are probably the best preventives and should be applied especially in young debilitated children.

Involvement of

per cent of cases.

a considerable pro

type, is usually permanent. Acute arthritis—a result of the initial septicæmia—often declares itself after treatment has stopped It rapidly responds to a second course of therapy.

Convalescence.—The patient may be allowed out of bed towards the beginning of the third week of illness. A lumbar puncture should be performed on or about the twenty-first day of illness, the best criteria of recovery are a normal cell count and a normal content of sugar in the fluid, which should be clear. The patient may now resume normal activities and a reasonably long holiday should be advised. Adult patients often complain of a general weakness for some time after their recovery; their relatives often complain of the patient's easy irritability. Such changes, however, gradually disappear.

ACUTE MENINGITIS DUE TO OTHER BACTERIA

Meningitis due to pneumococcus, streptococcus, staphylococcus and *H. influenzæ* is almost always secondary to some other focus of infection in the body. Should the bacteriological report incriminate one of these organisms, both sulphonamide and antibiotic therapy will be required. The treatment calls for the closest co-operation of physician, neuro-surgeon and bacteriologist, and such cases should rarely be treated outside of hospital The following are the main principles of treatment:

Sulphonamides—The dosage should be high and should be continued for ten days. Sulphadiazine is the drug of choice initially, but laboratory tests may indicate that the causative organism is more susceptible to some other sulphonamide.

Antibiotics.—Penicillin is given systemically in a dose of 100,000 to 500,000 units every four hours Intrathecal administration is also essential, the dose being 20,000 units once or twice daily. The systemic penicillin will take care of the primary focus of infection which nowadays rarely requires urgent inter- [illegible]

[illegible]

five days, but the state of the patient and the condition of the spinal fluid will [illegible]

chloramphenicol or erythromycin may be preferred for certain cases as a result of the initial sensitivity testing, but it is important to bear in mind not only the possibility of infection by initially resistant strains but also of the development, under treatment, of resistance to the antibiotic in use For this reason repeated changes of treatment for "panic" reasons unsupported by precise bacteriological data are to be condemned In guiding the patient through these hazards close co-operation with the bacteriologist is essential.

Relapse, Blockage and Brain Abscess—These complications are much more liable to arise from the organisms mentioned above than after meningococcal meningitis and must be kept constantly in mind There must be no hesitation in performing lumbar, cisternal or ventricular puncture, any indication of rising intracranial pressure, especially in streptococcal infections, should raise the suspicion of abscess formation. The co-operation of the neuro-surgeon is essential for success. (See section on Nervous Diseases, p 808)

CHRONIC MENINGOCOCCAL SEPTICÆMIA

This condition is particularly to be expected during epidemics Unfortunately, blood culture, which is the essential method of diagnosis, is not always [illegible]

headache, or skin rash

ACUTE MENINGOCOCCAL SEPTICÆMIA WITH ADRENAL HÆMORRHAGE

(See p 373)

TUBERCULOUS MENINGITIS

(See p. 132)

MUMPS

(Epidemic Parotitis)

incubation period varies from twelve to twenty-six days, but usually lies between seventeen and twenty-one days

Although the parotid is the gland most frequently involved, it is well to

The occurrence of a

Preventive Treatment.—*Specific Prophylaxis.*—Although the prevention

of infection in adult life is thus diminished.

General Measures —The patient must be promptly isolated. The quarantine period for mumps contacts is twenty-six days, but where the date of exposure is definitely known, an exposed child may safely attend school for the first ten days of this period In actual practice, provided a contact is examined daily and isolated on the first suspicion of illness, exclusion of contacts from school is quite unnecessary A child who has previously suffered from the disease may, for practical purposes, be regarded as immune and need undergo no restrictions. Adult contacts may continue their business activities. Women who are in the early months of pregnancy should not be allowed to come in contact with the disease.

Hot dry cotton-wool or hot fomentations applied to the swollen glands will help to relieve pain and local discomfort. The mouth should be washed out with a 1 . 5,000 solution of permanganate of potash or other mild antiseptic preparation four times daily.

Treatment of Complications.—Orchitis usually develops when the

parotid swelling is at its height and may be expected in ... per cent of males above the age of puberty.
with cotton-wool and the inflamed parts

Symptoms of abdominal pain and vomiting are usually due to pancreatitis. ... with limitation of ... the pain is severe,

Convalescence. ... the patient should be continued for one week after the parotid swelling has subsided. The minimum isolation period is fourteen days

POLIOMYELITIS

(Infantile Paralysis)

illness or there is a disturbance of varying clinical severity unaccompanied by paralysis There is no doubt that in some of these " minor " illnesses the virus actually reaches the central nervous system but the illness aborts without subsequent paralysis. That a considerable amount of unrecognized infection occurs in the community can now be demonstrated by the virologist who is able to show the presence of serum antibodies (a sound index of past infection) in a high proportion of the adult population—often, indeed, in people who are unaware of having encountered the infection.

The virus enters the body by the mouth, multiplies in the cells of the intestinal

... would appear that the fæcal excretion of virus is greatest in the most severe cases Virus is present in the stool of all paralytic cases, the excretion slowly waning over a period of eight to ten weeks In about half the patients, stool cultures become negative in three to four weeks

There are three distinct serological types of poliomyelitis virus, of which Types 1 and 2 seem to be the more frequent epidemic producers. The incubation period probably varies widely although in most cases it lies between seven and ten days

thus to prevent the disease in contacts along lines exactly similar to those which proved successful in measles. Such a measure was used on a very wide scale in

America with limited success. Although the concept is theoretically sound, it is not a practicable method of control and its use is not advocated.

A poliomyelitis virus vaccine which contains formalin-killed virus of all three types is now available. In its production an attempt has been made to choose strains which possess a high antigenic capacity but which are of reduced paralytogenic power. During the early days of poliomyelitis vaccination in America the presence in the vaccine of a live paralytogenic strain of Type 1 virus caused a number of paralytic cases—some of which were fatal. The improved methods of vaccine production and more elaborate preliminary testing before issue have removed this danger so that the antigens now in use are safe. Two injections of 1 0 ml. are given intramuscularly or subcutaneously at an interval of four weeks. This should be followed by a third injection six months later. As a means of producing individual protection the vaccine is effective, for all the evidence suggests that the risk of subsequently acquiring paralytic disease is reduced. The amount of unrecognised infection with poliovirus is not accurately known. However, as has been said, in some communities it is certainly considerable, so that a large proportion of the healthy adult population show antibody to at least one of the types. As a result it is not easy to state which age-group merits high priority for vaccination. Much work is being carried out on the production of immunity by means of the oral administration of strains of virus which do not produce paralysis—a form of vaccination which would use the natural pathway of infection and, if successful, would have much to commend it.

General Measures —By the time that a diagnosis of paralytic poliomyelitis is made it may be assumed that infection has been well distributed among the contacts This makes effective control very difficult. There is, however, agreement that the patient must be promptly and effectively isolated and this is best done by admission to an infectious diseases hospital. Children who have been in contact with the patient should be kept under strict medical surveillance for a period of three weeks from the date of last contact. Adult contacts may continue their occupation providing it does not entail mixing with children, as in the case of nurses and school-teachers. They should, however, abstain from all social activities for three weeks from the date of last contact, kissing or playing with young children must be strictly forbidden. Any form of strenuous activity should be avoided.

[illegible] ptoms [illegible] until [illegible] least one week.

During epidemics the practitioner should advise mothers to ensure that children are not over-active and that they secure adequate rest. A short period of enforced rest immediately after the midday meal is a sensible measure.

It is now accepted that certain factors provoke and determine the nature of the predominant paralysis For example, tonsillectomy may be followed by a severe form of bulbar infection. During periods of prevalence operations on the nose and throat should be countermanded. It has also been shown that intramuscular injections, especially alum-containing diphtheria and [illegible]

activity often precedes a severe paralytic attack. During epidemic periods more than normal attention must be paid to minor febrile illnesses Patients should

nor gamma-globulin has effect upon the course of poliomyelitis, for by the time a diagnosis has been made the virus is in the nerve cells and beyond the reach of antibody

General Management.—*The "Minor" Illness.*—It is easy to seem over-fearful of poliomyelitis, but there is no doubt that few infections rouse such

ness

the

pains

or weakness—the condition will only be recognized either when there is a history of contact with a case of paralytic illness or when the disease is known to be present in the district In such circumstances it is wise to adopt caution in dealing with minor febrile illnesses and to counsel complete rest It seems possible that strict bed rest in such cases may minimize, though it will not always completely prevent, subsequent paralysis.

The "Major" Illness—This may be suspected when there is extreme irritability, muscle tenderness or pain or obvious paralysis Spinal and neck

use of a "cage" to take the weight of bedclothes. When the patient is being treated outside of hospital, the advice of an orthopædic surgeon should be immediately obtained.

When the shoulder-girdle muscles are involved, the possibility of interference with respiratory efficiency must always be kept in mind Careful examination to exclude diaphragmatic paralysis must be made. The patient should be asked to count from 1 upwards to see how far he can get with a single breath. The test can be frequently repeated and forms a useful gauge of diminishing respiratory control It is important to differentiate between respiratory insufficiency due to lack of muscle power in diaphragm and intercostals from that due to obstruction of the airways by mucoid secretions from

adequate drainage, which is best obtained in the prone position with the foot of the bed raised. Suction of the pharyngeal secretions must be frequently carried out and every care taken to ensure a clear airway Contrary to the usual belief, these purely bulbar cases, when properly managed, will usually recover, the patient who is in greatest danger is the one in whom there is a combination of spinal and bulbar involvement, when the most skilled medical and nursing care is essential. All preparations must be made to maintain respiration

When all muscle tenderness has disappeared, simple splints (e g. Cramer

wire) should be applied under the guidance of an orthopædic surgeon, who should, in fact, be called upon to assist in the supervision of the case from the onset of paralysis The limb should not be encased in plaster but should lie in plaster "shells" or padded Cramer wire splints made to the individual's

transfer of the patient to an orthopædic hospital. It should be emphasized that careful attention to the paralysed limbs during the first six weeks is of paramount importance and makes a great contribution to the ultimate complete recovery of the patient

ORNITHOSIS

(Psittacosis)

Human infection with the viruses of ornithosis usually arises through contact with diseased parrots, budgerigars or other members of the parrot family, but the disease may also be contracted from infected canaries, pigeons, finches, or fulmar petrels. The bird may show signs of illness. On the other hand, apparently healthy home-bred birds may carry the virus and prove to be a very real danger. The virus is excreted in the bird's droppings, and the portal of infection in man is probably the respiratory tract. Human case-to-case infection has been suspected but not proven

The duration of the incubation period is uncertain, but may be seven days or longer.

Ornithosis is not a notifiable disease.

An acute febrile illness with combined typhoidal and pneumonic symptoms occurring in a person who is closely associated with parrots, pigeons, etc , is probably ornithosis The diagnosis can be confirmed either by the isolation of the virus from the blood or sputum, or by the complement fixation test.

Prevention and Control.—As a result of the epidemic of psittacosis in this country in 1930, the importation of birds of the parrot family was strictly controlled. Unfortunately, this policy has failed to banish the human disease. The simple and obvious method of prevention rests with the public, who if they do not wish to run the risk of psittacosis should not keep these birds in

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a diagnosis. Extreme care must be taken in handling and disinfecting all articles

ffective against infections

. daily, given by mouth at

six- to eight-hour intervals.

Although isolation need not be enforced, it is probably wise to regard the patient as potentially infective. Sputum, urine and stools should be disinfected.

RUBELLA

(German Measles)

Rubella is a virus infection, spread by direct contact and possibly by fomites. There is no information available regarding the conveyance of infection by carriers. Infectivity appears to be limited to the prodromal and early eruptive stages of the illness.

The incubation period is usually from fourteen to eighteen days, but may vary from twelve to twenty-one days

Rubella is not a notifiable disease.

Preventive Treatment.—Rubella in the first three to four months of pregnancy may cause changes in the fœtus and the baby may be born with congenital defects The common abnormalities reported have been congenital cataracts, deafness and cardiac defects This important fact must completely alter our outlook on this trivial disease On the one hand there is need to review the traditional meaasures in regard to quarantine, for, especially in girls, there is now every reason for encouraging infection in childhood Unfortunately, it is hard to interfere with established practice and school authorities are slow to adopt this new principle When a woman in the early months of pregnancy is exposed to the disease sero-prevention should be practised Gamma-globulin has been prepared from rubella convalescents and may be obtained from Blood Transfusion Centres If not available, ordinary gamma-globulin in double the dose advised for measles (*q v*) should be given

Curative Treatment.—Treatment is purely symptomatic. The patient should remain in bed until the temperature has subsided and the rash faded. The illness is usually so mild that the patient can be kept on an ordinary diet and no special treatment is required Complications are rare. Recovery is usually complete in five to seven days.

SCARLET FEVER

(Scarlatina)

Scarlet fever results from infection (usually of the throat) with *Str pyogenes*. It occurs only if the streptococcus produces the specific toxin in the host and if the host is susceptible to that toxin. The typical rash (and perhaps some of the [illegible]

clinical syndrome Many mild cases occur which are liable to be missed and spread the infection. People who have become immune to the toxin are not necessarily immune to streptococcal infection When they are infected, a streptococcal tonsillitis may occur, and such persons, perhaps even more than carriers, play an important part in the spread of the disease and render control virtually impossible.

Although infection very commonly occurs through the medium of the "missed case", the contamination of animate or inanimate materials by streptococcal discharges is also of importance Infected milk is a common cause of

epidemics. In hospital wards, the dust may contain streptococci, and measures to reduce dust form an important aspect of control. After recovery, cases both of scarlet fever and of tonsillitis which have not been specifically treated may continue to carry streptococci in the throat or nose. Nurses (especially midwives), teachers and individuals associated with the supply of milk should be subjected to detailed bacteriological examination after recovery from the infection and before return to work.

Scarlet fever has a short incubation period—from two to five days—and is a notifiable disease.

Prevention and Control.—*The Dick Test.*—This test, which is analogous to the Schick test (*q.v.*) measures the capacity of the individual to neutralize the erythrogenic toxin. The material used is Dick test toxin, and 0 2 ml. of this is injected intradermally into one forearm. The test must be read much earlier than the Schick test and twelve to eighteen hours is the usual time interval—a positive result (an area of erythema of 1 cm or more) indicating susceptibility to scarlet fever It must be emphasized that the result of the Dick test gives no indication of the individual's susceptibility to streptococcal infection but merely of his capacity to cope with the toxin

by

and

which is purely anti-toxic, will in the majority of individuals last for years, but has no effect in preventing other forms of infection with *Str. pyogenes.*

Passive Immunization.—The injection of a dose of scarlet fever antitoxin as a means of procuring passive immunity has nothing to commend it. As has already been pointed out, the subsequent immunity is only partial and other forms of streptococcal infection may still occur.

Sulphonamides.—Although the sulphonamides inhibit streptococcal invasion, their routine administration to prevent the occurrence of scarlet fever—of which the majority of cases run an uncomplicated course—is quite unjustified.

Penicillin—Systemic penicillin will clear streptococci from the throat and in ward outbreaks in hospital the spread of the organism is limited by this treatment In such conditions, with the patient under control, administration of oral penicillin V for five days usually suffices to break the chain of infection.

General Measures.—The patient must be promptly and effectively isolated. Children who are contacts should be excluded from school for one week after removal of the patient to hospital. When the patient is treated at home, some

A quarantine period of at least one week must be strictly enforced in the case of adult contacts whose occupation entails the handling of milk or other foods or close contact with children. Unless the serological type which infected the first case is known, the swabbing of contacts should not be encouraged. If typing can be carried out, the search has some precision and is then worth doing. It must be realized that a proportion of the normal population may be expected to carry hæmolytic streptococci in nose or throat.

If an epidemic of streptococcal infection is to be stamped out in a residential school or institution, typing becomes essential, so that cases of hæmolytic

streptococcal tonsillo-pharyngitis and carriers of the specific organism may be isolated. Bacteriological assistance must be employed as a routine measure.

Many practical problems involved in the effective control of scarlet fever have still to be solved.

Curative Treatment.—*Serum Treatment.*—The early intramuscular administration of scarlet fever (streptococcus) antitoxin (3,000 units) rapidly alleviates the toxæmic symptoms, and thus renders the patient more comfortable. Although antitoxin can prove life-saving in the hyper-toxic cases, these are now exceedingly rare and for the present mild form of scarlet fever the administration of antitoxin is unnecessary.

Chemotherapy.—Although, like sulphonamides, penicillin cannot have any effect upon the toxæmic element of the infection, it has a valuable place in the management of scarlet fever. The sulphonamides suffer from the fact that streptococcal invasion is so frequently followed by pus formation; and in the presence of pus, sulphonamide activity is diminished. Penicillin, on the other

thereby reduced.

The administration of Dover's powder with aspirin will help to allay head-

promptly burnt.

As a rule, after the administration of penicillin, the temperature rapidly subsides and the remainder of the illness is uneventful. In children, pain in the tonsillar lymph glands is frequently complained of and a warm woollen scarf is comforting. A daily inspection of the ear-drums, especially in young children, facilitates the early diagnosis of otitis media. It is well to remember that in children otitis is often painless.

Complications.—Otitis media, nephritis, arthritis, adenitis and rhinitis are complications, for the treatment of which the reader is referred to appropriate sections of this book. Nephritis is now recognized to be associated with infection by a few special types of *Str. pyogenes*—particularly type 12. The complication therefore tends to occur in certain epidemics only. Acute rheumatism, on the other hand, may occur after infection by any of the serological types.

Toxic Attacks.—Toxic scarlet fever, fortunately of rare occurrence in recent years, is characterized by an abrupt onset, a temperature from 105° to 107° F., persistent vomiting, profuse diarrhœa, delirium and extreme prostration; the rash is frequently inconspicuous. The onset of such symptoms in a child who has been in recent contact with scarlet fever is an urgent indication for

immediate intravenous administration of scarlet fever antitoxin in a dose of 20,000 units. Treatment with penicillin is then begun—using the antibiotic in aqueous solution intramuscularly at four-hourly intervals.

Convalescence.—Providing the condition of the myocardium and the pulse is satisfactory, patients with mild uncomplicated scarlet fever may be allowed out of bed on the seventh day of disease, and in suitable weather into the open air three days later; those suffering from severe or complicated attacks should be confined to bed for at least three weeks.

Carriers

The mere presence of *Str. pyogenes* in the fauces or nose cannot be regarded as a reliable index of infectivity. Nevertheless, a rich growth of this organism from either the throat or nose of certain persons, e.g. dairy workers, nurses, medical men, school-teachers, may reasonably be regarded as an indication for continued isolation until the carrier condition has ceased. A course of systemic penicillin in doses of 0.5 mega units per day for five days is usually effective. If this fails, tonsillectomy should be advised. Antiseptic applications to the fauces and pharynx are worthless.

SMALLPOX

(*Variola*)

Of recent years two distinct varieties of smallpox have occurred in Great Britain—variola major and variola minor. The latter was at one time endemic in certain parts of the country; the former is always imported from abroad. Clinically the two types can be similar, but whereas the death rate of major smallpox is around 15 per cent., that of minor smallpox rarely exceeds 0.2 per cent. The minor form is apparently due to a smallpox virus of low virulence and the disease breeds true. Vaccination is equally protective against both forms of the disease.

The virus of smallpox almost certainly enters the body via the respiratory tract. During the course of the infection, virus is discharged in the secretions of the mouth and nose and from the skin lesions. Bed-linen is thus heavily infected and the air of the room becomes charged with the virus. Although infection is most often from case to case, papers, clothing, etc., may all act as vehicles, for the virus appears capable of survival for long periods in the dry state. As a result, not only must the isolation of the case be complete but there must be the most stringent disinfection of all clothing and other articles in the sickroom.

The incubation period is usually twelve days, but may vary between ten and fourteen days.

Smallpox is a notifiable disease.

Prevention.—The control of smallpox is essentially a public health problem. The accurate diagnosis of the initial case or cases rests, however, with the practitioner, and herein lies a grave responsibility. Early diagnosis, followed by prompt isolation of the primary case, the immediate vaccination and continued supervision of all contacts, and thorough disinfection of the patient's house and its contents are the essentials of successful smallpox control. *The practitioner should not hesitate, therefore, to make immediate contact with an experienced consultant regarding any case which he has the least reason to suspect*

might be smallpox. The misdiagnosis of the initial case or cases as chickenpox has been the starting-point of almost every recent smallpox epidemic in Great Britain.

There can be no doubt as to the wisdom of promptly removing every case of variola major to hospital. Hospital isolation should be enforced during an epidemic of variola minor so long as accommodation is available In the event of continued spread of the minor form, circumstances may justify or necessitate home treatment These matters of policy are for the local Medical Officer of Health to decide

After the removal of the patient to hospital, every member of the family and every known contact should be immediately vaccinated. Children, unless recently successfully vaccinated, should be excluded from school for sixteen days from the date of last contact with the patient. Adult contacts who accept vaccination may continue their occupation, but should be examined morning and evening for a period of sixteen days. Adult contacts who do not accept vaccination should be strictly quarantined.

If a case of variola minor is treated at home, isolation of the patient should be strictly enforced and every member of the household vaccinated Current disinfection must be conscientiously performed

Vaccination.—In this highly effective method of prophylaxis against smallpox, introduced by Jenner in 1798, vaccinia, or cowpox, is inoculated into the human subject Vaccinia is now regarded as a modified form of variola virus resulting from its passage through animals.

The National Health Service Act in Great Britain has abolished compulsory vaccination in infancy, but since this is the only reliable prophylactic measure against smallpox, it cannot be too strongly recommended that infant vaccination be advised

Primary vaccination should not be performed until the fourth month of life, and should be postponed if the child is debilitated, febrile or has recently been exposed to infectious disease It should never be performed on an infant who is [illegible]

expelled from the tube by a rubber teat—such as that used on an infant's feeding-bottle; *the mouth must not be applied directly to the tube*

The usual site for vaccination is over the insertion of the left deltoid muscle, but for æsthetic and other reasons the inner and posterior aspect of the arm or the outer aspect of the thigh or leg may be chosen The skin should be cleansed with soap and warm water, wiped with ether and *dried carefully*. The multiple-pressure method is recommended. To perform the operation a drop of lymph is first expelled on to the cleansed area With the side of the tip of a Hagedorn needle firm pressures are made through the drop of lymph on to the underlying skin, the pressure exerted should be sufficient to mark the skin, but not to draw blood. For a primary vaccination 10 to 12 pressures are adequate, for revaccination 20 to 30 should be made Excess lymph may be blotted off immediately and no dressing is necessary This method has the advantage that it produces a minimal amount of trauma and therefore of local reaction and subsequent scarring. It does not give such a

long-lasting immunity as the older method, but since smallpox is no longer an endemic disease, the protection it affords is sufficient for most of the people in this country. When the maximum degree of protection against smallpox is desirable (in smallpox contacts), the number of insertions should be increased to two, situated at least 1 in. apart

The duration of immunity to smallpox after primary vaccination is variable. Good " takes " to revaccination may be obtained even after the lapse of only one year A distinction must be drawn between the results of primary vaccination and revaccination. In the former the resulting lesion does not reach a maximum until about the eighth day ; in the latter the maximum evolution is reached on the third to fifth day.

Both of these reactions indicate that the individual was susceptible to smallpox and has now bee

in revaccination to regard

maximum in twenty-four

interpretation is unacceptable, for there may be three other explanations. First, the vaccination may have been unsatisfactorily performed; second, the lymph may be inert, and third, the individual may be reacting merely to trauma or to the vaccine lymph The last may be excluded fairly easily by carrying out a control vaccination with heated lymph. The others can only be excluded by performing the vaccination at least three times , at the last insertion an entirely different site should be chosen.

In the event of exposure to smallpox, vaccination should immediately be performed unless there is reliable evidence of successful primary vaccination within the previous three years or successful revaccination within the previous five years. The important words in the last sentence are " reliable " and " successful ". In case of doubt, revaccinate. Owing to the risk of vaccinal encephalitis, slight as it may be, primary vaccination should not be performed in school-children or in adolescents unless they have been directly exposed to smallpox ; exceptions to this general rule are nurses and medical students—for the possibility of unsuspected contact in such persons is always present.

Successful vaccination within the first four days of the incubation period may prevent an attack of smallpox

Curative Treatment.—There is no specific treatment for smallpox. The constitutional disturbance of the prodromal stage is treated on the lines already laid down (p 1) The diet at this stage is limited to fluids, and water must be administered freely.

Neither the sulphonamides nor the antibiotics at present available have been found to influence the maturation of the rash of smallpox from the maculo-papular to the vesicular stage, even when therapy is begun in the pre-eruptive phase. The administration of antibiotics in adequate dosage may, however, be

goes steadily downhill, showing evidence of increasing toxæmia, presumably due more to the absorption of tissue breakdown products and widespread destruction of the epidermis than to any bacterial effects

General Management.—During the papular and vesicular stages of the eruption the regular application of an antiseptic dusting powder (Boric Talc Dusting Powder, B P.C.) or calamine lotion (B P.) will help to allay the skin

irritation. In variola minor such treatment will usually suffice, for in this form the rash often aborts, secondary fever is usually absent and the prognosis is uniformly good.

Iced compresses applied to the face and distal parts of the limbs, and frequently changed, will be found comforting in the confluent eruption of major smallpox. Prolonged warm baths, spraying with a 1 : 40 solution of phenol or smearing the skin with 3 per cent. carbolic vaseline are alternative methods of treatment. In children the arms may require to be splinted or the [illegible]

[illegible] with confluent cases of major smallpox can be masked to some extent by sprinkling eucalyptus oil on and around the bed The application of starch or linseed poultices spread thinly on lint will hasten the separation of the scabs, and subsequent tenderness of the skin can be alleviated by the application of sterile talcum powder or zinc oxide ointment The virus is suceptible to the action of [illegible]

Owing to the presence of the eruption on the mucous membranes, the eyes, mouth, throat, nose and larynx require careful treatment Drops of 20 per cent. [illegible]

[illegible] with two parts of water may be employed as a spray or mouth-wash. Frequent inhalations of steam, impregnated with Friar's balsam or creosote, help to alleviate laryngeal and bronchial symptoms. Dysphagia may be lessened by sucking fragments of ice or an amethocaine lozenge before each feed

The fluid diet of the prodromal period requires to be supplemented by soft solids during the eruptive stage. Fresh fruit juice drinks sweetened with glucose must be administered freely throughout the illness.

Complications [illegible] tracheotomy. [illegible] Keratitis [illegible], if the eyes have not been carefully treated from the first Myocardial damage is frequently present and strict bed rest must be enforced throughout Hæmorrhage, especially from the uterus, is fairly common in female patients with smallpox, and may necessitate transfusion with blood or plasma

Convalescence.—The patient should be kept in bed until the eruption has crusted and isolation must be continued until the last crust has separated from the skin This period varies from three weeks in mild cases to three months or longer in severe attacks. Detachment of the crusts can be hastened by [illegible]

[illegible] soap-and-water bath and shampoo precedes the transfer of the patient to a non-infected room in which he puts on clean clothes

In variola minor and in mild attacks of major smallpox convalescence is

usually rapid and the patient is fit for discharge from hospital or isolation as soon as he is free from infection. He may return to school or business in two to four weeks after release from isolation, but after severe attacks, several months may elapse before the patient is able to resume his normal activities.

TETANUS

The normal habitat of *Cl. tetani* is the intestinal tract of horses, cows and other herbivora. The bacilli are sometimes found in human fæces Heavily manured soil is particularly liable to be contaminated with the highly resistant *spores of the tetanus bacillus* *Introduced through a punctured wound* commonly made by a splinter or nail, the bacilli or spores—particularly in the presence of pyogenic infection, laceration of tissues or a foreign body—tend to multiply and produce the powerful toxin which acts on the nervous system.

Although the potential risk of tetanus following deep wounds is well

post-operative tetanus.

The length of the incubation period and the duration from the onset of symptoms until the appearance of definite spasms have both a very important bearing on prognosis An incubation period of less than seven days indicates a severe case When the prodromal period is less than twenty-four hours a fatal outcome is almost invariable.

Early diagnosis is very important Stiffness of the jaw, pain in the neck or back increased by manipulation and associated with the characteristic facial expression *should lead to immediate specific treatment*

Tetanus is not a notifiable disease

Preventive Treatment.—*Passive Immunization.*—The disease could be abolished by the routine use of a small dose of tetanus antitoxin when this is warranted by the circumstances mentioned above.

Passive immunization is an effective measure, but it must be understood that the method has its limitations. First, the passive immunization must be carried out at the time of injury. Delay is dangerous Secondly, passive

important, persons who have previously received horse serum in some form may develop serum sickness , such persons are liable to eliminate the antitoxin more rapidly, thus reducing the period of " cover ". To these factors must be added the doctor's natural reluctance to administer antitoxin when a wound is apparently trivial—yet such wounds may be infected by tetanus. The prac-

units intramuscularly) when it is indicated

Active Immunization.—As in diphtheria prophylaxis, the value of active immunization against tetanus by means of toxoid is obvious. Two injections of 1 0 ml. separated by an interval of four to six weeks produces a sound basic

immunity, and if this is followed by a third injection after a year or eighteen months the hazard of tetanus is virtually abolished. Active immunization is particularly desi
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Armed Forces,
and diphtheria toxoids is also available—and when these are used they should be obtained from reliable manufacturers and the directions for their use followed exactly. The use of a mixed diphtheria-tetanus toxoid in infancy, when the child is being immunized against diphtheria in any case, has much to commend it

When a person who has been actively immunized is exposed to infection, the antitoxin level in the blood can be boosted by the injection of a dose of 1·0 ml of toxoid. Such a person does not usually need antitoxin. However, when there is reason to suspect heavy contamination by tetanus, it is wise to give 3,000 units of antitoxin into one buttock and 1 ml. of tetanus toxoid into the other. The presence of antitoxin does not interfere with the production of antibody which results from the injection of toxoid.

Combined Active-Passive Immunization.—When the circumstances warrant the giving of prophylactic antitoxin and the patient has *not* been previously immunized, the method of combined active-passive immunization should be used. A dose of 3,000 units of antitoxin is given into one buttock, and then 1·0 ml. of toxoid is given into the other. Six weeks later the second dose of toxoid is administered.

Curative Treatment.—The four essentials in the treatment of tetanus are: (1) the early administration of an adequate amount of antitoxic serum; (2) thorough cleansing of the wound, (3) sedatives to abolish spasm and rigidity; and (4) adequate intake of food.

Antitoxic Serum.—The early administration of an adequate dose of antitoxin is the first measure, and 200,000 units should be injected intravenously. This antitoxin will neutralize only free circulating toxin and cannot affect such toxin as is already fixed in the tissues. Antitoxin administered late in the disease cannot have any curative effect, for nervous tissue damage is already beyond the reach of serum For this reason alone intrathecal injection of antitoxin should not be used.

Cleansing of Wound—Owing to the possibility of increased toxic absorption it is a wise procedure to delay cleansing the wound until after the intravenous administration of antitoxin.

Scabs and foreign bodies should be removed, penetrating wounds freely opened up and whitlows incised. After the evacuation of all pus and the removal of lacerated tissue, the wound should be gently syringed with hydrogen peroxide and dressed with light porous gauze. Dressings should be changed every four hours. Free drainage is essential, the wound being kept open and allowed to granulate from the bottom.

General or regional anæsthesia may be required. Local anæsthesia and cauterization of the wound are inadvisable because they are liable to cause necrosis of tissues which favours proliferation of bacteria. Although penicillin may be used to inhibit or to treat secondary infection, it has no effect upon the course of the tetanus infection

Control of Spasms.—In mild cases without convulsions 60 mg (1 gr.) of phenobarbitone administered every six hours is all that is required. If the

highly effective as a practical measure in controlling typhus. It not only simplifies disinfestation but affords a high degree of protection to the personnel. Details of its application are given on p. 232.

It is obviously important that a patient suffering from typhus fever should not be admitted to a hospital ward until he has been carefully disinfected of lice—which may be presumed to be infected with Rickettsia. The cleansing [illegible]

cent. emulsion of cresol in 5 per cent. soft soap solution.

Contacts are kept under daily observation for three weeks from the date of last exposure Adults, following disinfestation, may be permitted to attend business, but children should be kept away from school throughout the quarantine period.

Curative Treatment.—*Serum Treatment.*—Claims have occasionally been made for convalescent human blood or serum and for immunized horse serum. The former has been given intravenously in a dose of 200 ml., or intramuscularly in doses of 20 ml. or more daily. The horse serum is given intramuscularly in daily doses of 20 ml. for five days The value of serum therapy has, however, not been widely confirmed

Chemotherapy.—Chloramphenicol and oxytetracycline have both proved effective in the management of typhus. A total amount of 3 g. daily in divided dosage may be given orally for three to five days. In " scrub " typhus a single dose of 3 g is usually curative, but should the temperature rise on the following day, a further single dose may be necessary

General

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protected by active immunization and the use of a reliable insecticide. Skilled nursing is essential. The diet and management are on the same lines as advised for the treatment of a severe case of enteric fever.

Pyrexia, headache, insomnia and delirium call for frequent tepid sponging and the exhibition of hypnotics Retention of urine is commonly present and should be relieved by appropriate measures The myocardium suffers severely in typhus fever, and every precaution should be taken to conserve the patient's strength. Azotæmia is a feature of the severe case and a persistently high blood urea is a bad prognostic sign Dehydration and toxæmia call for daily intravenous infusions of 5 per cent. glucose saline by the drip method.

Complications.—Although complications are uncommon, laryngitis, bronchitis, broncho-pneumonia and myocarditis may give rise to anxiety during the acute stage of the illness Thrombosis in the veins or arteries, particularly in the lower limbs, is a feature of some epidemics.

Convalescence.—Strength is usually rapidly regained, but the reaction of the cardiovascular system to increased effort must be carefully watched. The patient may be permitted to sit up in bed one week after the temperature has settled, and may get up a few days later. The appetite returns early and the diet may be rapidly increased. As the patient may be regarded as non-infective from the time of delousing, he may be permitted to leave hospital when fully recovered, but should not resume work for at least another four weeks.

WHOOPING-COUGH

(Pertussis)

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infective during the catarrhal stage of the . (

diagnosis is very difficult. The causal organism is spread by direct contact, droplet infection and perhaps by fomites. Abortive and unrecognized attacks are common, particularly in adults, and frequently prove an unsuspected source of infection

possible on clinical grounds alone, but the onset of a

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these

are now less than they were. may be taken either through the mouth or the nose If a thin wire swab is obtainable, the nasal route is better *Isolation of the organism has been aided by the use of* special media. Although most infections are due to *H pertussis*, there is evidence that some infections are due to an antigenically distinct organism—*H. parapertussis* Other aids to diagnosis are of less value, complement-fixing antibodies, *for example, only appear late in the illness*, white cell counts marked lymphocyte preponderance) may prove useful in older

fants

n—The use of vaccines for

oversial subject. However, it

is now ciable degree of protection. Indeed, with certain vaccines 80 to 90 per cent of inoculated children are

c the infection arises in a vaccinated child, the

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known as the "Phase I stage of gro ,

genicity. The usual prophylactic course requires a total dosage of 60,000 to 80,000 million organisms given in three intramuscular injections at monthly intervals. *Difficulty may arise from the fact that the antigenically distinct* organism (*H. parapertussis*) can cause whooping-cough, immunity is specific to the type of organism injected (namely, *H pertussis*) so that failures may be due to infection with parapertussis strains

Wh cough vaccines have been prepared *in combination* with alum-

both laboratory evidence and field trials

heria-pertussis product gives a high degree

of protection against both diseases Thiomersalate is used as a preservative in these materials, as it has the least effect upon the antigens of *H. pertussis* The combined product may safely be kept in a single container. If combined immunization is to be carried out, the first injection should be given at the age of three months, for, if the whooping-cough vaccine is to afford maximum benefit, the earlier in life it is given the better. The course consists of three injections of 0 5, 0 5 and 1 ml respectively *with one month's interval between* them. Since the combined diphtheria-pertussis injection has been most frequently implicated as a provoking factor in poliomyelitis, it must not be used during periods of poliomyelitis prevalence

General Measures.—The general public, and indeed the medical profession, require to be educated to realize that pertussis is now the most serious infectious

excluded from such places as nursery schools during a quarantine period of three weeks.

Curative Treatment.—*Specific Treatment.*—The tetracyclines are effective in reducing the severity of the attack only when they are started early, that is, in the first fourteen days of the illness. A daily dose of 0·25 to 0·5 g. depending on age is indicated and should be continued for from seven to ten days. Recrudescence may occur when treatment is stopped prematurely. Once the whooping spasm is well established, antibiotics produce little or no benefit and should only be prescribed for the treatment of complications according to the normal indications.

General Management.—Even when antibiotics are used, reliance must still be placed on measures designed to lessen the severity of the spasms and perhaps to prevent lung complications. Isolation of the child from all contact with others, especially adults, may have some effect in reducing exposure to secondary infection. If the condition of the child permits, strict confinement to bed is unnecessary and may be unwise. Movement promotes aeration of the lungs and it is undoubtedly true that the occurrence of atelectasis is as much to be feared as broncho-pneumonia. For the same reasons the sickroom should be well ventilated, and indeed, if the weather permits, an hour or so in the open daily is beneficial.

When the paroxysms are at their height it is essential for the child to be

the back during the paroxysm assists the expiratory phase of the cough and encourages deep inspiration.

The feeding of the infant and young child presents a serious problem. Advantage may be taken of giving the child its food after a paroxysm; or of

lemon drinks flavoured with glucose.

If the paroxysms become severe and frequent, sedatives provide the only method of relief. For a child of one year one of the following may be tried—syrup of chloral hydrate, 0·6 ml (10 min.), syrup of codeine phosphate, 0·6 ml. (10 min.); Dover's powder, 30 mg. (½ gr.); or phenobarbitone, 10 mg.

toxicity. A preliminary dose of 0·1 ml. (2 min.) three times per day may need to be pushed to 0·5 to 0·6 ml. (8 to 10 min.) for satisfactory response.

It must be remembered that there is an undoubted nervous element in the paroxysm. Quietness in the sickroom is essential; any sudden disturbance of

occurrence, are not of serious import. Well-marked cardiac dilatation may occur in severe cases. Otitis media is not uncommon

For broncho-pneumonia, sulphadiazine and/or penicillin should be prescribed, though it should be remembered that many of the so-called broncho-pneumonias are in reality atelectatic areas with secondary infection. Chemotherapy has not produced such clear-cut benefit in the broncho-pneumonia of

complication by the prompt administration of a hot mustard bath with the application of cold water to the head

A few whiffs of chloroform will usually terminate the convulsion. Morphine sulphate should then be administered hypodermically, 2·5 mg. ($\frac{1}{25}$ gr.) to a child one year old, and the sedative effect continued by rectal chloral hydrate, 0·3 g. (5 gr.), which may be repeated as necessary. Lumbar puncture is a useful procedure when the convulsions are repeated. Repeated convulsions, however, are a grave prognostic sign

Convalescence.—Fresh air and plenty of good wholesome food are the essential requirements in convalescence. Care must be taken to protect the child against catarrhal infection or chill. If circumstances permit, a change of air to the seaside or to the country will prove very beneficial, particularly in patients with a persisting catarrhal condition of the lungs. Cod-liver oil and iron may be prescribed. The tendency of whooping-cough to reactivate a latent tuberculous process should be borne in mind

The paroxysmal cough may persist for months in some cases, but the duration of the cough is no measure of the infectivity. The child gradually loses its infectiousness from the time of appearance of the whoop; and as a rule may be regarded as non-infective four weeks after the appearance of that sign, despite its continuation.

SEPTICÆMIA

Bacteræmia—as distinct from septicæmia—is recognized as a normal phenomenon at the onset of enteric fever, meningococcal infections and as a transient condition following surgical procedures such as dental extractions.

clinical diagnosis cannot be exaggerated. This is the preliminary to blood culture and the identification of the causal organism Selective use of chemotherapeutic agents is then possible. Further, repeated blood culture during a course of treatment provides information of great importance in assessing the value of a drug ; the results also have prognostic significance.

As a general rule it may be said that, when the clinician is unable to identify the nature or cause of any severe infection, a blood culture should be taken before starting treatment. The special techniques necessary for the removal of blood for culture are described on p. 852.

The correct management of a case of septicæmia demands a proper under-
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or indicate
that it must be employed in a particular dosage Faced with such a case, the clinician must enlist the help of a bacteriologist.

SERUM REACTIONS

Refined serums have greatly reduced the risk of serum reactions. The fear of causing anaphylaxis therefore should not make the practitioner withhold serum when the need for it is clear For example, 4,000 units of diphtheria

than 5 per cent. of the cases to which they are administered. Nevertheless, in sensitive people, serum reactions do occur even with refined serums, and when large quantities of serum are given intravenously the danger of anaphylaxis is very real. The reactions which occur may be divided into two main groups :

1 Due to acquired or inborn sensitivity of the patient to foreign protein.
2. Due to causes other than allergy.

Reactions due to Serum Sensitivity.—Two main types of *general* reaction may be encountered, namely, (*a*) anaphylactic shock, and (*b*) serum sickness. *Anaphylaxis* is an immediate reaction, is of rare occurrence, but may prove rapidly fatal Dyspnœa, cyanosis, loss of consciousness and a thin, rapid pulse are the most common clinical manifestations *Serum sickness*, characterized by pyrexia, urticarial rashes, joint pains and lymphadenopathy, usually occurs from seven to twelve days after administration. In such patients there is, as a rule, *no history of a previous injection* of horse serum. *Accelerated serum sickness* occurs three to four days after administration and presents a similar clinical picture These patients usually have a history of a previous injection of horse serum

An intense form of *local* reaction is occasionally seen (*local anaphylaxis* or *Arthus's phenomenon*) A history of previous administration of horse serum, often within a comparatively recent period, is usually obtained. There is intense local œdema and hæmorrhage, and subsequently, there may be extensive sloughing of skin and even of muscular tissues

Tests for Sensitivity.—There is no satisfactory test for

reliance must be placed upon the answers to two questions, which must be

asked of patient or relative whenever a decision is taken to give serum. They are:

(i) Has the patient at any time in his life been given an injection of horse serum?

(ii) Is there any personal or family history of asthma, hay fever, infantile eczema or food allergy?

If the answers to these questions reveal that the patient is probably hypersensitive, certain precautions should be taken, and these are discussed below.

Methods of Administration of Serum.—When a decision is taken to give serum, the required dose must next be estimated. The decision in regard to dosage is important for it will to a large extent indicate the route of its administration for mild cases, the dose will be small and the intramuscular route will suffice, for severe cases, the dose will be large and the intravenous route will be desirable. The rules for the administration of serum may, therefore, be given under these two headings

Intramuscular Route.—The answers given to the two questions already stated will divide the patients into three groups

(*a*) Answers to both questions "negative". The injection of the required dose of serum is then undertaken The patient should, thereafter, be kept under

trial dose of 0 2 ml of serum subcutaneously and observed for half an hour. Should there be no evidence of any general reaction in this period, the main dose of serum may then be given intramuscularly Should there be any evidence of general reaction, a course of trial injections of 0 2 ml by the subcutaneous route should be continued at half-hourly intervals

(*c*) Answer to question (ii) "affirmative". It is in this group that special caution is required Adrenaline (1 · 1,000 solution) must be at hand and an injection of 0 5 ml to 1 ml given intramuscularly if any reaction is observed. A trial dose of 0 2 ml of serum diluted 1 . 10 in pyrogen-free distilled water should be given subcutaneously and the patient kept under observation for half an hour If there is no general reaction, a second injection of 0 2 ml. undiluted serum should be administered subcutaneously. If, after a further period of half an hour, no reaction has been noted, the remainder of the estimated dose can be given by intramuscular injection Should any reaction develop, it will be necessary to give the remainder of the serum by trial injections. A quick-acting anti-histamine (mepyramine maleate, 0 1 g) should be given by mouth at least half an hour before further injections are made.

There is no doubt that it is with patients who have an allergic history that the greatest risk arises *For this reason, it is of particular importance to ensure that allergic subjects are efficiently immunized against the two main toxic diseases, diphtheria and tetanus.*

Intravenous Route—Three points deserve acceptance as *absolute rules.* Firstly, no patient should receive an intravenous dose of serum as a preliminary step in treatment; an intravenous injection must *always* be preceded by an

before beginning the injection of serum. Thirdly, an intravenous injection should never be given to a patient who has a history of asthma or other allergic disorder, or who has shown a reaction to the trial doses described above.

Before serum is injected intravenously, it should be warmed by holding the syringe in the hand. It should be injected very slowly through a fine needle. The doctor must be prepared to stop the injection at once if there is any evidence of distress such as a short unproductive cough or cyanosis. In such an event adrenaline must be administered at once intramuscularly.

The above regimen has been described somewhat dogmatically, because it is felt that it should constitute a regular habit. The practice of so-called desensi-

system of trial injections suggested is an adequate safeguard against dangerous reactions; and the methods described are recommended as a standard practice

Treatment of Reactions.—As already stated adrenaline (1 : 1,000), 0 5 ml. to 1 ml., is the standard remedy for anaphylactic reactions. The injection should be given intramuscularly. The patient must be kept recumbent, the foot of the bed raised and hot-water bottles, additional blankets (or an electric blanket) used to raise the body temperature. Serum sickness can be very upsetting to the patient, although not itself dangerous. Here again adrenaline is indicated; 0 25 to 0 5 ml. should be injected every few hours to abolish urticaria and relieve itching. The irritable rash may also be soothed by calamine lotion to which phenol (2·5 per cent.) may be added for its anti-pruritic effect. Aspirin, 0·3 to 1 g. (5 to 15 gr.), usually relieves the joint pains and general malaise. Antihistamine drugs are worthy of trial, but they act only by preventing *further* exacerbations of urticaria.

Reactions not due to Allergy.—*Vasovagal Attacks.*—Very rarely the patient may collapse
is suffering from a
the face, bradycardi
of lowering the patient's head to improve the circulation to the medulla and the administration of diffusible stimulants. Occasionally it may be necessary to inject adrenaline. Measures described for the treatment of shock may also be indicated.

Thermal Reactions.—These reactions occur within thirty to ninety minutes of the injection of serum, and can be recognized by the presence of chill (rigor or shivering), rise in the temperature, malaise and sometimes nausea and vomiting. The rigor is followed by sweating. Thermal reactions usually occur in those who have been given serum intravenously.

The chances of a thermal reaction are greatly reduced (1) if scrupulous attention is paid to the preparation of rubber tubing, syringes, needles, etc , used for the injection of the serum; (2) if refined and concentrated serum is employed, for experience has shown it to be free from thermogenic substances; (3) if serum is administered very slowly.

During the stage of chill the patient should be kept warm with hot blankets and hot bottles. Hot fluids should be given along with 1 g. (15 gr.) of aspirin repeated, if necessary, in one hour. If the temperature rises excessively, tepid sponging is often beneficial.

T. ANDERSON.

CHEMOTHERAPY

INTRODUCTION

IN 1935 Domagk demonstrated that an azo-dye (Prontosil Red) possessed marked anti-streptococcal activity. This activity was soon shown to be due to *p*-aminobenzenesulphonamide or sulphanilamide. Later, other compounds were synthesized containing this molecule, and the scope of sulphonamide chemotherapy was thereby enlarged. This great advance was quickly followed by the development by Florey and others of Fleming's discovery of the antibacterial properties of penicillin, an extract of the mould *P. notatum*. Spectacular as these discoveries were, however, a wide range of bacteria—notably the gram-negative bacilli—still remained unaffected, and an intensive search was undertaken to produce materials capable of dealing with them During the past twelve years, out of over 3,000 antibiotics which have been isolated, a small proportion—some fifteen to twenty—have survived clinical evaluation. Their use has brought almost every human and indeed many animal diseases of [illegible]

[illegible] of an infection that [illegible] This may induce [illegible] etter; and such an attitude can, in time, result in complacency. In consequence, what might be termed "careless chemotherapy" often results. In this term must be included not only the administration of the different agents in ineffective dosage but also their employment for conditions which are already known not to benefit from their use There are inherent dangers in such actions. Ineffective treatment may not only fail to overcome the infective process but may so alter the clinical picture as to render diagnosis difficult Bacteriological examinations may be [illegible]

[illegible] infection under treatment come in contact with minimal and non-lethal doses and so become resistant to its action. Thus, in many parts of the world the endemic strain of *gonococcus* is sulphonamide resistant; an increasing proportion of *Staph. aureus* (particularly in hospital wards) is found to be resistant to the antibiotics in common use; while the appearance of resistant forms of *M. tuberculosis* is already posing serious problems to the clinician and to the [illegible]

[illegible] forms of chemotherapy.

1. **Is the diagnosis clearly established clinically?**—It is not suggested that a full bacteriological examination is always a necessary prelude to efficient therapy. In many cases, such as erysipelas and pneumonia, a correct clinical diagnosis implicates a limited range of organisms and indicates the use of a particular form of chemotherapy. But where the etiological agent is in doubt, treatment should not be started until appropriate steps have been taken to enable a correct bacteriological diagnosis to be made. Pyrexia is not a diagnosis and there is no justification for the indiscriminate use of potent chemotherapeutic substances simply because the patient is febrile. The adoption of this rule alone [illegible]

2. [illegible]
said, [illegible]
other agent. But virus infections are not susceptible and it therefore follows that in the great majority, where no bacterial complication is present, chemotherapy is unjustified.

3. **Which chemotherapeutic agent should be used?**—Some infections may be treated effectively with several of the substances, and it is of little [illegible]

control quickly, lack of toxic effects and cost.

4. **What dosage should be used?**—The dangers of ineffective dosage have already been mentioned Although much remains to be done to establish the optimal dosage of some of the antibiotics, it is sometimes desirable to start treatment with a large or " loading " dose Thereafter, the material should be given at regular intervals. For the majority of infections, prolonged treatment is unnecessary and undesirable. The course of treatment should not as a rule be less than five days, and, apart from certain well-defined exceptions, should not exceed ten days.

5. **Has the chosen treatment any harmful effects?**—When the therapeutic benefits are contrasted with the toxic effects there can be no doubt that the actual dangers are slight An important side-effect, however, of any form of chemotherapy is the alteration which it may induce in the micro-flora of the person treated. It is necessary to be on the outlook for these secondary changes as they sometimes explain the apparent failure of therapy.

MODE OF ACTION OF CHEMOTHERAPEUTIC SUBSTANCES

The introduction of the sulphonamides occurred at a time when attention was being directed to cellular metabolism and, *in particular, to the* precise nutritional requirements of bacteria The bacteriostatic activity of the sulphonamides gave further stimulus to these investigations and, as a result, what might be called the principle of competitive interference was enunciated. It was shown that *p*-aminobenzoic acid was an essential metabolite for certain bacteria and that sulphanilamide competed with this material for the possession of receptors on the bacterial body. A quantitative relationship was established between these two substances and it became clear that the beneficial action of the chemotherapeutic agent could be " blocked " by the presence of a specified amount of the metabolite. Since then, the nutritional importance of folic acid has been demonstrated and the fact that *p*-aminobenzoic acid plays an

important part in the chemical structure of pteroylglutamic acid has undoubtedly given further confirmation to the principle. The substances produced from sulphanilamide also form part of the chemical structure of material known or suspected to be essential metabolites. Although, for most of the chemotherapeutic agents, the interference mechanism has not been adequately established, there seems little reason to doubt that it will prove to be of a similar nature.

This important fundamental work has tended to focus attention on the

incomplete and that an essential factor in the recovery of the patient is the stimulus he can supply towards his own cure. With many infections successful phagocytosis of the dead or maimed bacteria is an important aspect of the struggle, and although it is difficult to define the terms, what may be called tissue or cellular resistance on the part of the host forms an essential factor in his recovery. Furthermore, it may be suspected that materials which so profoundly affect the nutrition of unicellular organisms such as bacteria may be expected to have at least some effect on the cells of the host In many infections cure is established so rapidly that treatment need not be unduly prolonged

immediate response of some infections to penicillin (e.g pneumonia) has anything to do with the production of specific antibodies It has been shown, in a few infections, that these are in fact present during convalescence and that the use of specific antisera produces no improvement in the speed of cure; but the subject has not as yet been adequately investigated. There is, however, some evidence that antibiotics, whose action is mainly bacteriostatic, may produce a more permanent cure when they combine with the patient's own naturally acquired antibody.

Such considerations may appear to be of more theoretical than practical importance, but as our knowledge expands, it seems likely that they will become of increasing significance It is already true to say that improvement in the results of treatment of many acute infections depends as much upon the discovery of substances which will enhance the response of the host as upon the discovery of new and more potent remedies. One important aspect of this is the value of cortisone in the treatment of certain fulminating infections. Its administration appears to enhance the patient's resistance and to maintain him until the chemotherapeutic material has brought the infecting agent under control.

SULPHONAMIDES

THE AVAILABLE COMPOUNDS

Sulphanilamide itself is now rarely administered, mainly because of its narrow therapeutic range Its freedom from renal complications, however, gives it a limited field of usefulness in certain urinary infections The com-

life such as meningitis, relatively large doses may be given during the first twenty-four hours. On the other hand, in the elderly patient in whom cardiac and renal insufficiency may coexist, any increase in dosage should always be accompanied by strict instructions regarding fluid intake and output. The dosages suggested in the table can be continued for a period of ten days, but, *in the great majority of cases, treatment should be completed by the fifth to seventh day*

The dosage of succinylsulphathiazole and phthalylsulphathiazole is approximately double that of the other sulphonamides. Thus, in adults, a daily dose [illegible] example, up to 18 g.

[illegible] passage through the kidney makes it unnecessary to use a high level of dosage for the treatment of urinary infections Indeed, the possibility in such cases of an accompanying defect in renal function should always occasion caution. As a general rule it is desirable to precede sulphonamide therapy for a period of twenty-four hours with high dosage of alkalies; thereafter 3 g. daily of sulphonamide will usually suffice. In such infections the need for repeated bacteriological examination is emphasized.

Parenteral Administration.—The occasions for intravenous or intramuscular administration of sulphonamides are few, but when it is considered necessary, as for example in fulminating meningococcal meningitis, the preparation of choice is " Soluthiazole ", of which 5 ml is equivalent to 1 g. of sulphathiazole.

Local Application.—Because of the danger of local sensitization, sulphonamides should not be used as salves or ointments though sulphacetamide can be used for eye drops.

INDICATIONS FOR SULPHONAMIDE CHEMOTHERAPY

Some of the newer antibiotics, because of their wide antibacterial activity, seem likely to supersede the sulphonamides as the treatment of first choice for many infections Nevertheless, the sulphonamides still offer a simple and completely effective method of treatment for quite a wide range of acute infections.

They constitute the first line of attack on infections of the urinary tract. The [illegible] ained in the urine is adequate to [illegible] tions Failure to obtain a sterile [illegible] a full examination of the urinary tract, for it will usually reveal an obstructive or other organic lesion. Infections by organisms other than *E. coli* are probably best dealt with by one of the antibiotics, and the advice of the bacteriologist should be sought.

Sulphonamide constitutes part of the therapeutic regimen for all forms of acute meningitis Meningococcal infections are in fact unique in this respect; for this organism is so highly sensitive to sulphonamide action that so far no other method of treatment has proved superior. In the other forms of meningitis due to *streptococcus, pneumococcus, H. influenzæ* and *Staph. aureus*, sulphona- [illegible]

[illegible] the Sonne varieties, but in some regions the prevalent strains have developed

resistance to sulphonamides so that the drugs are inactive. The salmonella organisms which cause food-poisoning are usually completely resistant. Although the poorly absorbed compounds were originally introduced for this type of infection, clinical experience indicates that the results obtained with

Sulphonamide is effective also as a routine treatment for erysipelas.

TOXIC EFFECTS

Common but of Little Importance.—*Malaise, Cyanosis, Vomiting.*—The administration of sulphonamides produces in most patients a general drowsiness and ill-defined malaise so that mental concentration becomes more difficult. Such complications only assume importance when the drugs are given to ambulant patients. Cyanosis is rarely produced by the sulphonamides now commonly employed. Gastro-intestinal upset is occasionally encountered, and apart from the discomfort to the patient has the only serious sequel that an unknown amount of the dose is lost if vomiting persists Under such circum-

heading may be included drug fever with or without the appearance of a skin rash. Although these may constitute the main manifestations, sensitization involves a generalized humoral and tissue reaction. Sensitization may occur in

received sulphonamide in the past, although there may be no history of a reaction. The third form occurs about the tenth day of treatment. The fever may reach 100° to 102° F, and remains high so long as the use of the sulphonamide is continued. After the drug is stopped, it may be two to three days before the temperature returns to normal

The rashes vary in character, but usually consist of small, pink, maculopapules which fade on pressure Conjunctival congestion often serves to increase the resemblance to rubella or measles The distribution is widespread, but tends to be more profuse on the extensor aspects, especially in the neighbourhood of the joints Sulphathiazole may produce a sparse nodal eruption which bears a strong resemblance to erythema nodosum The rashes are usually irrit

mic

or other of the antibiotics should be substituted

Renal Irritation.—Renal irritation is most likely to arise if the patient has been unconscious, if he is sweating profusely, or if the fluid intake has been low. The occurrence of microscopic hæmaturia indicates that caution is required. It is not, in itself, sufficient reason for immediately stopping treatment, since, if prompt measures are taken, the hæmaturia disappears. The immediate necessity

is to see that the patient is given by mouth during the next twelve hours a *minimum* of one pint of bland fluid for every gramme of drug in the daily dose. In addition to this, the urinary output *must now be measured accurately*. During the ensuing twenty-four hours a *minimum* of 1,500 ml. (50 fl. oz.) must be passed.

Obvious hæmaturia is an exaggeration of the previous complication. Treatment must be stopped and, during the next twelve hours, the patient must absorb, by mouth or other route, a minimum of six pints of fluid. A single oral dose of sodium bicarbonate (2 to 4 g.) should be given by mouth. When further chemotherapy is essential, a suitable antibiotic should be substituted.

Crystallization, of course, will not occur if the fluid intake and output is properly controlled. In temperate and cold climates this will usually be simple, for most of the fluid output is through the kidneys. In warm climates, however, where perspiration is excessive, urinary output must receive more attention The amount to be aimed at is 1,500 ml. (50 fl. oz) in the twenty-four hours. When there is doubt about the fluid intake, administration of alkalies is a useful precaution because it raises the *p*H of the urine and the sulphonamides are more soluble in an alkaline medium One final point may be noted: with high dosage, crystals will often be seen in urine after it has been allowed to stand for some time; provided the urinary output is normal, their presence is of no clinical significance.

Rare but Dangerous.—*Urinary Suppression.*—Hæmaturia results from irritation of the urinary tract by the deposition of sulphonamide crystals; should crystallization become excessive, actual blockage of the renal collecting tubules, the pelvis of the kidney or the ureters may occur, giving rise to a mechanical stoppage of urinary flow. The occurrence of anuria or marked oliguria necessitates immediate cessation of sulphonamide therapy. To begin with, fluids by mouth must be forced, and an intravenous infusion of one pint of sterile normal saline solution should be given. Unless urinary flow is re-established very quickly (within four to six hours) further excessive administration of fluids is unwise as it will only lead to generalized œdema or to œdema of the lungs. The management of such a case does not differ from that of patients suffering from suppression of urine from other causes (see p. 714).

Blood Dyscrasias.—When the toxicity of the sulphonamides is discussed, attention is usually focused upon this group of complications despite the fact that they are rarely encountered. Purpura, hæmolytic anæmia or agranulocytosis may arise, and although an excessively long course of therapy is the usual cause, such changes have occasionally occurred during the first five days of treatment and after comparatively small dosage.

PENICILLIN

GENERAL CONSIDERATIONS

Despite the discoveries of new antibiotics—discoveries which have brought under control infections beyond the range of penicillin—it is still true to say that penicillin remains the best of the antibiotics. Its freedom from toxic side-effects is alone a major advantage, while susceptible bacteria, with the exception of *Staph. aureus*, do not easily acquire resistance to it. It is therefore rarely justifiable to withhold it as a method of treatment of any infection which is caused by an organism generally considered sensitive to its action.

When penicillin was first introduced it was the custom to divide micro-organisms into two classes—those susceptible and those resistant to it. But with penicillin, and indeed with all the antibiotics, this is an over-simplification. Bacteria should be regarded as ranged in a "spectrum", at one end of which are placed the highly sensitive organisms and at the other the highly resistant. Each antibiotic has its own antibacterial range, and it is their overlapping which renders practically all bacterial infections amenable to treatment.

ABSORPTION AND EXCRETION

After intramuscular injection of an aqueous solution of penicillin G, diffusion into the blood stream is rapid so that a maximum concentration is reached in about thirty minutes. Renal excretion is unfortunately almost equally rapid, and within a short period, which varies with the size of the dose, the antibiotic can no longer be detected in the blood stream. Oral administration has to overcome two difficulties: firstly, although absorption does take place from the upper part of the small intestine, there is considerable individual variation in the ability to absorb the substance, due to such variable factors as gastric acidity and motility and the presence of food in the stomach; secondly, the production of penicillinase by intestinal secretions and bacteria may destroy a considerable amount of the drug. These difficulties have been overcome by the introduction of penicillin V (phenoxymethyl penicillin) which is well absorbed after administration by mouth and produces satisfactory concentrations in the blood. Generally speaking, however, the blood levels are never high so that oral administration is undesirable when the nature of the infective process indicates that a high concentration of penicillin should be maintained in the tissues. Nevertheless, this method of administration deserves more attention than it has received, for it proves adequate for many simple uncomplicated infections by highly susceptible organisms.

From the blood stream penicillin diffuses freely into the tissues, but is obstructed by most of the healthy body membranes. Thus it does not pass readily through the pleura, pericardium, peritoneum or synovial membranes. In particular, it does not penetrate the healthy blood-brain barrier, although, when inflammation of the meninges is present, this barrier is less complete. When infection is shut off in such sites, therefore, penicillin, to be successful, must be injected locally.

METHOD OF ADMINISTRATION AND DOSAGE

In considering the method of administration and dosage, any idea that there is a general or optimum standard should be discounted. Different species of bacteria vary in their susceptibility so that infections due to one will be brought under control with comparatively small doses, while others require intensive therapy. Even strains of the same organism may show considerable differences in their sensitivity. Further, it seems possible that some infections are best treated with a sustained low blood concentration, whereas others respond better when the doses are spaced out so that periods occur when there is little or no penicillin in the blood stream. Fortunately the commonest infecting agents—*Staph. aureus*, *streptococcus* and *pneumococcus*—are, in the main, extremely sensitive, so that intermittent administration usually suffices. It should be appreciated that with such infections it is wrong to think that "if a little is good, more must be better". Except in special circumstances, as in the treatment

of infections due to relatively resistant organisms such as *Str. viridans*, no advantage is to be gained by excessively high blood concentrations.

Quite apart from the sensitivity of the infecting bacterium, there must also be an appreciation of the nature of the infective process. Diffusion into many of the tissues is excellent, but barriers to the passage of the antibiotic, both natural and due to the infective process itself, may exist. The relative impermeability of the blood-brain barrier has already been mentioned; and yet when because of previous sulphonamide sensitization the need perhaps arises to treat a case of meningitis with penicillin, huge doses (of the order of 6 to 8 mega units per day) are necessary to ensure that an adequate concentration reaches the meninges. Therefore, attention must not be directed solely to the attainment of some theoretically optimum blood level, but to ensuring that penicillin reaches the bacteria at the site of the infection in adequate concentration. In the end it is the concentration in the infected tissue which matters. Sometimes this will be achieved best by local injection, although such a method is not always practicable.

The following are the different forms of penicillin available.

(*a*) **Benzylpenicillin.**—This is the form which is most readily available and is used for the preparation of aqueous solutions. Before administration the required dose is dissolved in a small quantity (1 to 2 ml.) of distilled water.

Dosage.—Clinical experience has shown that for the majority of the common acute coccal infections excellent results may be obtained by administering intramuscularly a dose of 200,000 to 500,000 units twice daily. When it is desired to attain high local concentrations the interval between doses may be reduced to a six-hourly schedule; each dose should then be of the order of 100,000 to 200,000 units. For infections due to resistant bacteria a daily dose of 6 to 12 million units may be required and may be used with safety.

This preparation is also suitable for injection into infected spaces. Intrathecal administration, for example, is essential in certain meningeal infections. As a [illegible] hould be the [illegible] ty-four-hour [illegible] a) a dose of 500,000 to 1,000,000 units should be injected into the cavity after the purulent contents have been aspirated. The required dose should be dissolved in an amount of distilled water approximating to that of the pus withdrawn; in the case of empyemas, however, 20 to 50 ml. will usually suffice.

(*b*) **Procaine Benzylpenicillin.**—The procaine salt of penicillin has a low solubility and is slowly absorbed. It has been prepared in a variety of ways of [illegible]

penicillin for administration as an aqueous suspension. The procaine salt is absorbed more slowly, and as a result, instead of the rapid fall in the blood level in three to four hours obtained with aqueous solutions of crystalline penicillin, the concentration gradually falls during a period of twelve to twenty-four hours, so that there may be demonstrable antibacterial activity in the blood at the end of that time. By combining the procaine salt with crystalline material, a high initial concentration is obtained for a short period followed by a longer period—up to twenty-four hours—at a lower level. Such preparations have therefore found a wide acceptance in practice. All the materials are satisfactory, but, in

general, the straightforward aqueous suspensions should be preferred. It has not been proved that the delayed absorption confers any real advantage over twice-daily injection of the aqueous solution or oral administration of phenoxymethyl penicillin

Dosage.—The preparations of procaine penicillin contain 300,000 units per ml.; when crystalline penicillin is added, the additional dose is 100,000 units per ml. A single injection of 1 ml. every twenty-four hours should be adequate for most infections.

Toxic effects.—The administration of aqueous solutions of procaine penicillin has been occasionally followed by more or less severe reactions of a sensitization character, with collapse, disorientation, tachycardia, sweating and severe malaise.

(*c*) **Penicillin Esters.**—The hydriodide of the di-ethyl aminoethyl ester of penicillin G may have value because of its affinity for pulmonary tissue. It has been used with advantage in acute exacerbations of chronic bronchitis and in some cases of bronchiectasis It is not superior to other methods of treatment of pneumonia.

Dosage.—The usual dose is 500,000 units at twelve-hourly intervals.

(*d*) **Oral Penicillin.**—The oral administration of crystalline sodium penicillin has proved effective in many infections of a simple character. The oral route, however, had serious drawbacks because of the large dose required and the uncertainty of absorption in any particular patient Phenoxymethyl penicillin has now been used extensively by the oral route and its efficiency in the treatment of many infections is beyond doubt Satisfactory blood concentrations are obtained by the administration of 200,000 to 400,000 units at four-hourly or six-hourly intervals For severe infections, particularly in the elderly, an initial intramuscular injection of aqueous penicillin may be given to secure rapid control of the infecting agent Thereafter oral administration of phenoxymethyl penicillin may be used to complete the treatment It has a particularly useful place in the treatment of infants and young children.

Dosage.—A dose of 200,000 units every three or four hours is essential.

(*e*) **Benzathine Penicillin.**—This is a useful preparation for achieving an adequate, prolonged antibacterial action in mild streptococcal infections by a single intramuscular injection

Dosage.—The dose is 300,000 to 600,000 units, and the effective duration of the penicillin activity is about fourteen days The most serious disadvantage is the local pain sometimes experienced after the injection

(*f*) **Penicillin Ointment.**—Ointments are usually dispensed with a content of 25,000 units per g They are of value in many local infections, for example, of the skin and eye The period of administration should not be prolonged beyond five to seven days, for, as with sulphonamide, there is a danger of local sensitization. When treatment is stopped, it is desirable in practice to see that the remainder of the ointment is destroyed, self-medication—unknown to the practitioner—may be prolonged and a puzzling dermatitis produced.

(*g*) **Penicillin Lozenges.**—There is no justification for local oral therapy, and the use of lozenges—or of chewing-gum containing penicillin—should be condemned.

Use of Renal Blocking Agents.—The excretion of penicillin by the kidneys is almost entirely through the renal tubules Certain chemicals (e g " Carona-

mide) have been produced which compete successfully with penicillin for tubular excretion, thus diminishing the loss of the antibiotic and increasing its concentration in the blood. Apart from a limited usefulness in the treatment

chemicals carry the risk of inducing sensitization and it is therefore undesirable to use such substances except under rigorous control.

TOXIC AND SIDE-EFFECTS

When penicillin is administered in aqueous solution intramuscularly, it is almost entirely free of deleterious effects. There is no known toxic dose for man

Like most chemical substances, however, it produces sensitization reactions. As a rule these manifest themselves as skin rashes—usually of urticarial type. The incidence of reactions seems much lower than with other forms of chemotherapy. An interesting feature of such sensitization reactions is that their appearance is sometimes delayed for as long as five to six days after treatment has been stopped. There has been a recent tendency to believe that an increasing proportion of individuals have acquired sensitization to penicillin and react anaphylactically to a single injection. This is not the writer's experience.

INDICATIONS FOR THE USE OF PENICILLIN

As a generalization, which of course requires qualification, it may be said that penicillin is the treatment of choice for all *severe* pyogenic coccal infections. Although sulphonamides produced excellent results in such diseases as pneumonia and erysipelas, penicillin is undoubtedly to be preferred when treatment is started late, when, on account of age, there may be anxiety as to toxic effects or when sloughing or pus formation is already present. Pneumococcal and streptococcal infections with septicæmia can be brought under control rapidly—often it would seem with the first injection.

The treatment of staphylococcal infections requires the most careful consideration Even among the general population, from one-fifth to one-third of *Staph aureus* may be expected to show some degree of resistance. But when

of first choice. Since staphylococcal infections can frequently run a fulminating course, it is important that the incriminating organism should be tested for sensitivity to several antibiotics when first isolated, so that the most suitable agent may be used.

In many parts of the world the development of sulphonamide-resistant gonococci has caused penicillin to become the standard treatment for gonorrhœa. In contrast to the great susceptibility of the gonococcus to penicillin, infections with another gram-negative coccus—the meningococcus—are comparatively resistant to penicillin so that sulphonamides still constitute the most effective treatment. In some of the other forms of acute meningitis penicillin is often an essential part of therapy, and must be administered intrathecally as well as intramuscularly. Finally, the value of penicillin in the treatment of syphilis is now definitely established.

Even when the initial treatment involves some other specific therapy, penicillin can exert a valuable secondary effect. Thus in severe cases of diphtheria, once the toxæmia has been modified by antitoxin, chemotherapy should be instituted in order to eradicate the infecting agent more rapidly. In this way the patient may be rendered non-infectious quickly and the "carrier" state in convalescence avoided. The same is true of gas gangrene, and to some extent of tetanus. But in all of these infections neutralization of toxin is an essential prerequisite.

The fact that penicillin is effective even in the presence of pus or tissue breakdown products make it valuable in the treatment of abscess, empyema and other collections of pus. The majority of cases of post-pneumonic empyema can be successfully treated by lavage and instillation of penicillin (1,000,000 units in 20 to 50 ml.) into the pleural cavity. Open operation is seldom necess-
for the small, well-localized empyema; and even when
the subsequent healing is rendered

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,000 units may be inhaled over a
such a form of therapy has on occasion a valuable place
in the treatment of acute respiratory infections. In chronic pulmonary infections (for example, bronchiectasis) it must be used with caution and carefully controlled by bacteriological examination of the sputum. In such cases it will often be found that inhalation therapy merely produces a temporary change in the bacterial flora; many of the organisms are naturally penicillin resistant or rapidly become so.

STREPTOMYCIN

GENERAL CONSIDERATIONS

Streptomycin is more readily affected than penicillin by the *p*H and consistency of the fluids in which it is acting. An acid *p*H lowers its activity, and since tissue destruction is often associated with a trend to the acid side, this may explain, at least in part, its disappointing effect in many suppurative conditions. Unlike penicillin, too, its activity varies with the number of organisms present, and in this respect it resembles the sulphonamides.

Although streptomycin has a somewhat broad antibacterial range, weight for weight it is a less potent antibiotic than penicillin, for even susceptible organisms may require fairly high concentrations for their subjection so that the curative doses in the different infections need to be high. Although it has a limited place in general chemotherapy, its real importance rests on its activity against *M. tuberculosis*. It has two serious disadvantages: firstly, the comparative ease with which resistant strains develop, and secondly, that it has undoubted toxicity. For these reasons streptomycin therapy must be thoughtfully planned.

ABSORPTION AND EXCRETION

After intramuscular injection, streptomycin is rapidly absorbed and diffuses satisfactorily from the blood stream into most of the body tissues. Like penicillin it does not readily penetrate the intact blood-brain barrier, but, when the meninges are inflamed, satisfactory cerebro-spinal fluid levels may be attained. It is excreted through the kidney, but its rate of excretion is slower than that of

penicillin so that the interval between injections may be considerably greater. It is not absorbed after oral administration and exerts a temporary effect in reducing the number of bacteria in the fæces. Unfortunately re-colonization by resistant forms occurs very quickly.

DOSAGE

Simple aqueous solutions are employed, made up prior to use by the addition of sterile distilled water or normal saline solution There are two main routes of administration—intramuscular and intrathecal The preparation of the solution for intrathecal injection particularly must be carried out with the strictest asepsis, and it is desirable that each dose be dispensed in a separate ampoule. In view of the rapidity with which organisms become resistant to streptomycin, its topical application in the form of powders, salves and ointments is undesirable.

The maximum tolerated dose of streptomycin is probably not much more than three times the effective dose for most acute infections. Since it is desirable to avoid so far as possible the rapid development of bacterial resistance, acute infections are best treated with a short course lasting from three to five days and with a daily dose of 1 to 3 g given in divided amounts at intervals of four to six hours But when treatment must be prolonged over weeks or months, as in tuberculosis, the daily dose for an adult should not exceed 1 g. The daily dose should be proportionate to the age and weight of the patient and for infants and children is usually estimated on the basis of 40 mg per kg body-weight. It is now usual to give the daily dose in one injection Intrathecal administration, even of pure streptomycin, produces a meningeal reaction, with pleocytosis and increase of protein content. It should therefore only be given after careful consideration, for once it has been injected subsequent examinations of the cerebrospinal fluid are of limited value. The initial intrathecal injection should not exceed 50 mg and in children under the age of one year may be kept at this level throughout treatment. In older children and adults the amount can be increased over two or three days to 0·1 g. and retained at that level. One intrathecal injection per day suffices.

The emergence of strains resistant to streptomycin constitutes one of the [illegible]

a comparison may be made between the two strains Valuable time may thus be saved in deciding whether treatment should be repeated or recourse made to some alternative method of chemotherapy Certain devices have been shown to delay or prevent the appearance of resistant organisms Combination with other forms of chemotherapy is especially important; for example, with penicillin in the treatment of *H. influenzæ* infections and with para-aminosalicylic acid (PAS) or isonicotinic acid hydrazide (INAH) in the treatment of tuberculous conditions In the chemotherapy of pulmonary tuberculosis streptomycin must never be given alone.

TOXIC EFFECTS

Sensitization reactions similar to those resulting from sulphonamides and penicillin may be encountered Although these reactions can be very severe it

may be necessary in infections such as tuberculous meningitis to continue treatment despite their development. Control of the anaphylactic aspect of the sensitization with adequate doses of antihistamine drugs is worthy of trial, although their efficacy is diminished once the sensitization reaction has begun.

Most importance attaches to the neurotoxicity of streptomycin resulting in vestibular dysfunction and deafness The changes in vestibular function are a serious hazard. With patients in bed it may be difficult to decide when vestibular symptoms appear, and in any case it is usually necessary to continue treatment despite their presence. Once established, the defect is persistent and there may be considerable disturbance of balance, especially in the dark and when walking over soft or uneven surfaces. Children and young adults usually learn to compensate quickly and adequately so that serious disability does not result; but in older patients compensation is less easily established and the permanent

impossible. Although it has occurred after systemic treatment alone, it is much more frequent after intrathecal therapy. In consequence it has been encountered most often in patients treated for tuberculous meningitis. Three factors

associated with neurotoxicity than streptomycin and for this reason should never be given intrathecally.

Although the deafness may be limited to certain tone frequencies, it is usually complete. Under the latter circumstances, particularly with young patients, no time should be lost in obtaining the assistance of a speech therapist.

INDICATIONS FOR THE USE OF STREPTOMYCIN

Acute Infections.—Streptomycin has proved effective in the treatment

essential to secure careful concurrent bacteriological control and to keep in

sulphadiazine has been effective

Streptomycin has a place in the treatment of gram-negative infections of the urinary tract It should not, however, constitute the first line of attack and should only be prescribed after bacteriological examination of the urine has indicated that the organisms are sensitive In chronic infections or where there is evidence of some defect of the urinary tract, streptomycin is not advisable, for relapses, usually with resistant organisms, are common

Reference has already been made to the increase in the occurrence of penicillin-resistant staphylococcal infections mainly as a result of cross-infection in hospitals Since streptomycin is also commonly used in hospital wards, concomitant resistance to streptomycin is usual.

Successful results have sometimes been obtained in gram-negative infections of the respiratory tract due to such organisms as *H. influenzæ* and Friedlander's bacillus. Treatment should be started early before suppurative changes have occurred; unfortunately, by the time a bacteriological diagnosis is made, tissue breakdown has often begun and chemotherapy proves unavailing.

Streptomycin has a limited place in the treatment of acute infections. There are, however, many infections which, because of the rapid development of resistant strains, are *not* likely to benefit from streptomycin treatment. In ... fections of the bowel such as ... it should *not* be used in the ... ch as bronchiectasis; and it should *not* be used as a local ointment or dressing for acute infections

Tuberculosis.—The use of streptomycin in tuberculosis is fully discussed on p. 125.

THE TETRACYCLINES

Oxytetracycline, chlortetracycline and tetracycline are three analogues which have great similarity. firstly, in the wide range of their antibacterial activity; secondly, in their capacity to produce resistant strains of micro-organisms with an acquired resistance common to all three; and thirdly, in the pattern of side-effects which they may produce. The broad spectrum of their activity means that their antibacterial effect is indiscriminate Although this must never interfere with their proper use, they should not be employed when another remedy will be equally effective.

The chemotherapeutic spectrum of the tetracyclines is wide. They are effective against the common gram-positive organisms—*pneumococcus, streptococcus* and *Staph aure*
such as *E. coli, salm*
importance is their
uninfluenced by chemotherapy, namely, those due to Rickettsiæ and to the psittacosis-lymphogranuloma group of viruses Claims for the efficacy of oxytetracycline in such virus diseases as mumps, infectious mononucleosis, chickenpox and herpes zoster have not been substantiated. The only justification for their use in such virus infections is to treat secondary bacterial invasion. Much unnecessary medication would be saved if it were fully realized that chemotherapy is completely ineffective in such conditions as the common cold and uncomplicated influenza

DOSAGE

For effective treatment a daily dose of 1 0 g. is adequate Nothing but harm results from overdosage, for some of the toxic effects—in particular gastro-intestinal irritation—are due to this cause An initial loading dose is unnecessary. The daily dose may be divided into two and prescribed twelve-hourly. The use of lactobacillary preparations (milk or cheese) has been advo-

UNWANTED SIDE-EFFECTS

The tetracyclines effect a considerable change in the bacterial flora of the mouth and bowel which, in part, explains the frequency with which gastro-intestinal symptoms may arise during their administration. In this respect oxytetracycline is more upsetting than chlortetracycline, and tetracycline is the least toxic. This supports the view that local irritation plays a major role in inducing these side-effects. It has been suggested that some of the symptoms arise from vitamin deficiencies induced by the lethal effect of the drugs on the bowel flora, and there is no doubt that animal experiments have been conducted which support this contention. These experiments, however, are somewhat artificial and bear little resemblance to the conditions of normal therapy. In most acute infections the period of therapy should not exceed four to five days, and it is hard to believe that a severe degree of hypovitaminosis could develop in this time. In practice, the administration of vitamin preparations does not prevent the appearance of all varieties of side-effects. Their routine use is not recommended.

The main effect upon the microflora which accompanies oxytetracycline therapy is overgrowth of *C albicans* and *Staph. aureus* The former (which [illegible]

Superinfection with staphylococcus has proved rather more important. The main site of this superinfection is the bowel, but it has been observed in the throat, the sputum and the urine. The staphylococci are resistant to the tetracyclines. *Staph aureus*, is of course, normally present in the fæces of a proportion of persons; during tetracycline therapy, however, a moderate to heavy overgrowth may be observed. In a hospital ward, where many of the patients are receiving the antibiotic, this has given rise on occasions to outbreaks of staphylococcal infection, the most serious aspect of which is the occurrence of a profuse cholera-like diarrhœa from which a pure culture of staphylococci can be obtained. Some of these patients have died partly from the acute onset of dehydration and electrolyte disturbances, but probably also from absorption of toxic substances from the bowel. Such a condition almost certainly arises in hospital wards as a result of the cross-infection with staphylococci which is constantly occurring. In general practice, where each patient is treated more or less in isolation, the possibility is greatly reduced. None the less, it is a side-effect the seriousness of which cannot be over-emphasized. Not the least [illegible]

or a combination of these may be expected in about a quarter of patients treated.

It is unusual for the complaint to be so severe that the patient refuses to take the antibiotic. The stools become more bulky even when there is no actual diarrhœa, but in about half of the patients it may be expected that the consistence of the stool becomes softer than normal and that more than one stool is passed in the day. A few patients complain very bitterly of a severe burning pain on defæcation. The tongue often acquires a glossy atrophic appearance, and actual

most striking abnormality of

due to fungal overgrowth.

n the female—is of severe

irritation and pruritus around the perineum which can persist for weeks after treatment has stopped.

Such complications are encountered as the result of treatment with all the tetracyclines As has been said, they occur more frequently with oxytetracycline and chlortetracycline than with tetracycline itself, but this may merely reflect the fact that experience of tetracycline is of shorter duration. The danger of overdosage has already been emphasized

Mention must also be made of the complication—increasing in its frequency—which is common to all chemotherapeutic agents, namely, sensitization. A greater proportion of such cases may be expected as the use of tetracyclines increases. Treatment should be restricted to four or six days at the maximum. Local skin sensitization from the use of salves or ointments containing oxytetra-

treatment is completed, ointments containing antibiotics should be destroyed by the doctor

INDICATIONS FOR THE USE OF THE TETRACYCLINES

The tendency to regard the tetracyclines as the antibiotics of first choice for all types of infection should be discouraged For most of the common infections other forms of chemotherapy are available which are just as effective and freer from side-effects.

Rickettsial infections (which may be encountered in Great Britain mainly in the form of Q. fever) and psittacosis constitute absolute indications for one of the tetracyclines.

Other important applications include the treatment of infections caused by penicillin-resistant staphylococci. It may be assumed that staphylococcal infections acquired in hospital will be penicillin-resistant and some other antibiotic should be used pending reports on the precise sensitivity of the organism If, of course, the tetracyclines are also being used frequently, they may likewise prove ineffective, which is a good reason to employ them sparingly, especially in hospitals The increasing frequency with which organisms are isolated with a varying pattern of resistance also emphasizes the importance of obtaining adequate specimens for bacteriological examination before starting the treatment of severe cases. Although common sense dictates that the physician will often need to begin treatment on the strength of a correct clinical diagnosis and before any assistance can be offered by the bacteriologist, this should not absolve him from the responsibility, in cases where a precise bacterio-

logical diagnosis can be made, of submitting the necessary specimen for examination.

Pneumonia is now often regarded as an indication for the use of the tetracyclines although there are really no grounds for such an assumption. Penicillin proves adequate for nine cases out of ten; and a mixture of penicillin and streptomycin—particularly useful in infancy where a staphylococcal infection may be feared—will prove adequate for most others. That vague clinical description known as "primary atypical pneumonia" should be discarded. Such a diagnosis lacks ætiological precision; the clinical picture may be produced by viruses, by Rickettsiæ, sometimes by bacterial pathogens and, one suspects, by a bizarre host reaction of a non-infective character. It seems possible that the good results sometimes reported from the use of a tetracycline are explained by the specific ætiology of a group of cases or by the presence of a secondary bacterial invader susceptible to the tetracycline used

Pertussis is responsive to the tetracyclines, and in view of the severity of

for a period of seven days.

Bacillary dysentery is an example of a condition in which bacteriological cure may be achieved more rapidly by the use of tetracyclines and this is especially indicated in the treatment of a food handler. A low level of dosage is adequate—5 to 10 mg per kilo per day By contrast with dysentery, the salmonella food-poisoning infections have proved completely resistant to this treatment.

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the simple acute infection in the child or young adult due to *E. coli* clears rapidly with sulphonamide and streptomycin In the older person, however, there is often some complicating pathology, the infection may be mixed and unusual bacteria may be encountered. Study of the sensitivity pattern of the organisms may suggest one of the tetracyclines as the best treatment. The second con-

treatment is not to be regarded as a panacea for these cases, there is no doubt of its value in some individuals

CHLORAMPHENICOL

ABSORPTION AND EXCRETION

oral

abo

hours. Chloramphenicol diffuses readily into most of the body tissues and appears in reasonable concentrations in, for example, the bile and cerebrospinal fluid Of particular interest in view of its rather unpleasant taste is the fact that it is well absorbed from the rectal mucosa, so that, in very young children,

is not absorbed when given by mouth, it has proved useful in the treatment of intestinal infections. Like polymyxin, it is effective in eliminating the typable strains of *E. coli* in infantile gastro-enteritis. It is less efficient in shigella infections, although, when other methods of treatment have failed, neomycin (sometimes combined with a sulphonamide) is worth a trial. It has not proved successful in eliminating the organism in salmonellosis.

Neomycin has been used successfully in the treatment of skin infections Since it is never used systemically there is a possibility that its topical use will be less frequently associated with sensitization.

The oral dose is based on a scale of 50 to 100 mg. per kilo body-weight per day.

MYCOSTATIN

(*Nystatin*)

The fact that administration of the " broad-spectrum " antibiotics encourages the growth of *C. albicans* in the respiratory and intestinal tracts has already been mentioned It must be emphasized that, as yet, there have been few recorded examples in which this superinfection has endangered the life of the patient Nystatin has a decided anti-fungal action, but since very little is absorbed from the bowel, its principal effect is in decreasing the amount of monilia in the intestine. It has also a place in the local treatment of superficial infections of skin or mucous membrane.

Tablets of 500,000 units are available, and the usual adult dose is three of these daily.

T. ANDERSON.

CORTICOTROPHIN AND CORTISONE

IT MAY BE premature at this stage to attempt a summary of the status of

divergences of opinion as to the justification for their use and as to their mode

an attempt to summarize our present attitude to them would appear to be desirable. The initial period of excessive optimism, when cortisone was regarded by many as a wonder drug, was followed by one of pessimism as its formidable side-effects were recorded and it was generally feared that these effects might far outweigh its usefulness This, in its turn, has given way to the current view that cortisone, though not a general panacea, is in fact a most valuable addition to the armamentarium of the clinician, which must, however, be employed with wisdom and propriety

The use of most potent drugs carries with it the risk of inducing harmful side-effects. This is particularly so in the case of cortisone, which, besides modifying disease processes, exercises a profound influence on the physical and even the mental attributes of patients Further, its immediate symptomatic effects in various conditions are often so dramatic and apparently beneficial that the doctor may be tempted to employ it in circumstances in which its use may be unjustifiable from a long-term point of view. Cortisone is a two-edged

various diseases it is necessary to make some brief reference to their general effects on metabolism and on the function of different organs and tissues. Attention will be paid mainly to those effects which have definite clinical applications.

PHYSIOLOGICAL ROLE

EFFECTS ON STRESS AND ON CARBOHYDRATE, PROTEIN AND ELECTROLYTE METABOLISM

Stress.—It is now well recognized that the normal organism responds to stress or injury in a fairly characteristic manner, a response which has been referred to by Selye as the " alarm reaction ". The features of this reaction which are common to almost all types of bodily insult include an impaired carbohydrate tolerance, a negative nitrogen and potassium balance, retention of sodium and chloride, eosinopenia and lymphopenia, dissolution of lymphoid tissue and thymic atrophy. Simultaneously there is evidence of enhanced

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CORTICOTROPHIN AND CORTISONE

IT MAY BE premature at this stage to attempt a summary of the status of corticotrophin and cortisone in therapeutics, for many aspects of the subject are as yet in a state of flux. Thus, experienced observers still disagree as to the efficacy of these hormones in this or that condition, and there are wide divergences of opinion as to the justification for their use and as to their mode

desirable. The initial period of excessive optimism, when cortisone was regarded by many as a wonder drug, was followed by one of pessimism as its formidable side-effects were recorded and it was generally feared that these effects might far outweigh its usefulness This, in its turn, has given way to the current view that cortisone, though not a general panacea, is in fact a most valuable addition to the armamentarium of the clinician, which must, however, be employed with wisdom and propriety.

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adrenal cortical activity manifested by ascorbic acid and cholesterol depletion of the adrenal glands, adrenal hypertrophy, elevated levels of blood corticoids and increased excretion of corticosteroids in the urine. As nearly all these changes can be produced by the injection of corticotrophin and as none of them occurs in the hypophysectomized or adrenalectomized animal it was natural to assume that they were the direct results of an increased secretion of corticotrophin in response to stress, and hence of an increased activity of the adrenal cortex. This assumption may be unwarranted, since it has been claimed that *adrenalectomized animals maintained on a constant small dose* of cortisone, insufficient in itself to produce an effect on nitrogen or electrolyte metabolism or on lymphoid tissue response, reacted to stress in just the same way as controls with intact adrenals. Under the experimental conditions no change in adrenal steroid level could occur. Hence the adrenal hormones may be essential for the alarm reaction without being primarily responsible for it. All that we can say with certainty at present is that this metabolic response, which depends on the presence of adrenal hormones, is necessary in order that certain tissue defence mechanisms may develop satisfactorily, and in saying this we are merely confessing our ignorance

Carbohydrate Metabolism.—Cortisone affects carbohydrate metabolism in various ways. Gluconeogenesis from protein is stimulated so that liver glycogen stores are increased. There is a decreased sensitivity to insulin so that

treatment It may be that those who develop glycosuria in response to cortisone are in reality pre-diabetics. The clinical converse of this diabetogenic effect is to be seen in the increased sensitivity to insulin of patients suffering from hypopituitarism and Addison's disease, and in the improved sugar tolerance which occurs in the few diabetics who develop these disorders or who have been subjected to hypophysectomy.

Renal lesions resembling those of the Kimmelstiel-Wilson syndrome have been produced in experimental animals following prolonged administration of the hormones. Further, the characteristically large, bloated, waterlogged babies of diabetic mothers exhibit many of the attributes of Cushing's syndrome, and increased amounts of corticosteroids have been reported in the amniotic fluid of such fœtuses. Lastly, retrogression of severe diabetic retinopathy has been noted in a diabetic patient after the onset of Simmonds' disease, and it has been claimed that retinopathy and nephropathy have been checked following hypophysectomy. These findings suggest that adrenal cortical activity may play a part *in producing some of the complications of* diabetes. It is also known that both hypoglycæmia and ketosis stimulate adrenal cortical activity, so that it is reasonable to suppose that patients with poorly controlled unstable diabetes are subjected to frequent episodes of hypercorticism, which may partly explain the known correlation between the incidence of diabetic complications and poor control of the disease.

Protein Metabolism.—By stimulating the conversion of protein to carbohydrate, large doses of cortisone induce a negative nitrogen balance, but

the increased

protein catab

impaired and

to the slow healing of wounds which has been demonstrated frequently in the experimental animal but which is rarely encountered in the cortisone-treated patient.

Sodium and Potassium Metabolism.—Large doses of cortisone cause potassium loss with sodium retention and a consequent tendency to œdema A low salt, high potassium intake is therefore desirable for patients who are likely to require cortisone in high dosage for more than a few days. Under such [illegible] the hormone being used for its physiological rather than for its pharmacological effects.

PHARMACOLOGICAL ROLE

EFFECT ON INFECTION, INFLAMMATION AND ALLERGY

Infection.—The effect of adrenalectomy on resistance to infection showed that the absence of the adrenal cortex rendered the subject unduly susceptible to a variety of toxic and infective agents, as is well known to clinicians with experience of Addison's disease. Administration of cortisone to those patients in physiological doses restores normal resistance. Thus, shortly after the introduction of the hormones for clinical use, investigators were so impressed with their beneficial therapeutic effects on certain infectious diseases that their initial experiments were originally designed to test their protective or curative value in bacterial and viral infections It was soon demonstrated, however, that the doses required to suppress symptoms, far from having any such beneficial effects, actually aggravated infections of all kinds—pyogenic, tuberculous and viral. The ordinary symptoms of fever and toxæmia are suppressed by the hormones, so that the relationship between the host and parasite is altered, and the parasite flourishes without immediate reaction in the tissues or damage to the host. Within a few hours of death a patient may appear to be in good health, despite the presence of an overwhelming septicæmia. Equally remarkable is the absence of tissue reaction and damage as demonstrated either by gross or microscopical inspection. Thus severe infection may occur in patients undergoing treatment with the hormones, the usual evidences of which may be entirely masked, so that the infection may be overlooked and no remedial measures taken Further, chronic or dormant pre-existing infections may be aggravated or reawakened. Dissemination of tuberculous infection, in some instances without previous clinical evidence of active tuberculous disease, has been repeatedly reported. Lastly, there are clear indications from experimental work that organisms and viruses which are harmless for certain hosts may rapidly become lethal when the host is receiving corticotrophin or cortisone.

The mechanisms by which the hormones may produce susceptibility to infection are: (1) inhibition of inflammation, including decrease of capillary permeability and decrease of fibrogenesis; (2) the production of a negative nitrogen balance; (3) the inhibition of reticulo-endothelial activity leading to decreased antibody formation; (4) reduction of the capacity of phagocytes to digest bacteria.

It is clearly necessary to consider whether the hormones could be used solely for their beneficial symptomatic effects during treatment with very large doses of

antibiotics as a *means of shortening the acute toxic phase of* such infections as peritonitis, meningitis and septicæmia, thereby saving life and shortening convalescence.

Inflammation.—The anti-inflammatory effects of cortisone, by means of which it alters the clinical manifestations of a large number of diseases of apparently unrelated ætiology, appear to be entirely non-specific. It reduces cellular exudate, diminishes abnormal capillary permeability, inhibits the formation of new vessels and of granulation tissue and suppresses the fibroblastic reaction of repair. The doses required to modify the reaction of the tissues to inflammation in this way are considerably *greater than the amounts secreted* endogenously by the adrenal glands. They are pharmacological rather than

[illegible]

increases tissue permeability A similar increase in permeability occurs in the presence of inflammation, and its reduction by cortisone may account for part, at any rate, of [illegible]

Allergy.—

tion, but it is

action, except perhaps in the case of acquired hæmolytic anæmia. The extent *of antibody inhibition is in general quite inadequate to explain the dramatic* therapeutic effect of cortisone in clinical allergy in which symptoms and signs may be banished in a few hours. This strikingly beneficial clinical therapeutic effect contrasts strangely with the inability of cortisone to inhibit allergic reactions when induced experimentally. The difference may be due to the ameliorating effect of cortisone on the *inflamed site produced by the allergic reaction* as opposed to its lac[illegible] artificially produced in normal tissue. [illegible] reaction *per se* [illegible] produces a marked clinical remission in hay fever but fails to inhibit the skin reaction to an injection of the allergen responsible for the hay fever. On the other hand, when the skin itself is the site of the allergic disease, cortisone abolishes the cutaneous manifestations such as giant urticaria, the clinical analogue to the weal and flare reaction to injected histamine, which latter is [illegible]ffected by cortisone.

ntigen to the skin of

reaction, occurring

[illegible] type reaction, in which the

diminish the delayed reaction to bacterial antigens, including tuberculin. In this respect its action contrasts with that of the antihistamine drugs which [illegible]

differences between the prompt and delayed reactions to antigens may [illegible]

elucidate the mechanisms by which cortisone reduces the inflammatory response to a variety of stimuli.

In summary, then, it would appear that the most important therapeutic action of cortisone is to inhibit the inflammatory response of tissues to infective, toxic or allergic agents, and this suppressive action occurs irrespective of the primary cause and is entirely non-specific.

EFFECTS ON ORGANS AND TISSUES

The Adrenal and Pituitary Glands.—The amount of hormone secreted [illegible]

[illegible]

mechanism appears to operate when cortisone is given therapeutically; it depresses the function and reduces the size of the adrenal cortex with consequent failure of its hormonal secretion. Cessation of treatment is followed by a resumption of cortical function, but if treatment has been prolonged, this may take some time

Cortisone has also been shown to depress the production of corticotrophin by the pituitary gland It has been suggested that the secretion of the other anterior pituitary hormones may be similarly affected, but the evidence for this is inconclusive.

The Skin.—Cortisone may cause hirsutism of the face, arms and back, though it sometimes leads to some loss of scalp hair. Thinning of the epidermis and impairment of wound healing have been reported frequently in animal experiments, but in man impaired healing is encountered only occasionally. Acne vulgaris and reddish or purple striæ like those seen in Cushing's disease are sometimes produced during prolonged cortisone treatment There is also an accelerated blood flow in the skin capillaries, increased skin temperature and sweating, and reduced serum production. As has been said the weal and flare histamine reaction and the allergic eczematous response to patch tests are unaltered, but the delayed tuberculin response is reduced. The inhibitory [illegible]

[illegible]

tamination with melanophore hormone, is not seen during treatment with cortisone.

Bone.—The most important effect of cortisone on bone is the impairment of bone growth in young animals In elderly patients undergoing prolonged treatment there is a tendency to cause osteoporosis, which may occasion collapse of the vertebrae

Blood Pressure. [illegible]

[illegible]

retaining properties

The Brain.—Most patients develop some degree of euphoria on starting treatment, which may be of advanta e in counteracting the depression of toxic

states. On the other hand, cortisone exaggerates neurotic, psychotic or epileptic tendencies and should only be employed for very compelling reasons in those with an unstable mental background. Psychoses arising during the course of treatment usually subside when it is discontinued, though months may sometimes elapse before the mental state returns to normal.

The Stomach.—*Even after vagotomy the secretory functions of the stomach* are stimulated by cortisone and an exacerbation of the symptoms of peptic ulceration, including gastro-intestinal hæmorrhage and a reactivation of healed ulcers, is not uncommon Perforation of peptic and colonic ulcers—particularly gastric ulcers—occasionally results from such treatment, and as the signs and symptoms of the resulting peritonitis may be masked the diagnosis is rendered particularly difficult.

CONTRA-INDICATIONS TO TREATMENT

*If treatment with the hormone is continued over a long period with con*siderable doses, some signs of hypercorticism are unavoidable—particularly the moon face. A formidable list of toxic side-effects appears in the literature, but it must be remembered that many of these were encountered in the early days of treatment when very large doses were the rule. By using a smaller dose, however, it is often possible to achieve considerable, though not complete, suppression of the manifestations of the disease while avoiding the more serious repercussions of hypercorticism. When cortisone is needed to save life, the contra-indications to its use become relatively unimportant. Further, the dangers may be considerably reduced if specific treatment of the underlying *disease is given coincidently—for instance, anti-tuberculous chemotherapy* in a patient with a tuberculous history, and increased insulin dosage in the case of a diabetic. Nevertheless, the presence or even the history of tuberculosis,

[illegible]

employed in small doses for replacement [illegible]
should be taken before starting treatment to exclude pulmonary tuberculosis.

CORTISONE OR CORTICOTROPHIN?

[illegible] are similar but

[illegible]

action Corticotrophin stimulates the whole adrenal cortex, eliciting the production in addition to cortisone of a variety *of other hormones such as the* mineralocorticoids and androgenic ketosteroids In contrast, the administration of cortisone results in a depression of the whole adrenal cortex, thereby depriving *the body of cortical* hormones other than the administered cortisone. It is therefore surprising that there are not more numerous examples in clinical practice in which corticotrophin proves more effective than cortisone, and vice [illegible] are rare and are often due to the fact that

[illegible] n equivalent *and compar-*
[illegible] be effective and cortico-
[illegible] mportant advantage over

corticotrophin that it is active when given orally.

DOSAGE AND METHODS OF ADMINISTRATION

Corticotrophin is inactive when administered by mouth. Moreover, studies of its behaviour in the plasma have shown that its existence in the blood in an active form is only very transient, and that it is quickly inactivated. Thus, when the original preparation was injected intramuscularly it had to be given in divided doses three or four times during the day. The suppressive daily dose was usually about 100 mg *Rapid* intravenous injection is less effective than intramuscular injection, but slow intravenous-drip transfusion is capable of

effective in half the dosage of the short-acting compound For maintenance purposes these preparations are often adequate when injected only twice or thrice a week

The standard oral preparation is tablet of cortisone acetate (B P Addendum 1955) containing 25 mg of the drug, each tablet costs about one shilling. Injection of cortisone acetate (B P Addendum 1955) is a suspension of cortisone in saline (25 mg per ml) for which the only suitable route of administration is by intramuscular injection In general, cortisone is best given by the mouth, but patients who are vomiting, comatose or under general anæsthesia require parenteral therapy The hormone acts more quickly and for a shorter time when it is swallowed than when it is injected, and the interval between successive doses should be six hours. When given by injection, the effect lasts for twelve to twenty-four hours and the equivalent daily dose is about 20 per cent. less than the oral one.

The recognition that slight changes in the structure of the steroid molecule of cortisone may vary its clinical and biochemical effects has led to the clinical trial of a number of variants The first of these to be successful was hydrocortisone (Kendall's compound F), which became available in 1951. The action of both hormones is similar, but hydrocortisone is more potent. It is obtainable as a solution in 50 per cent. alcohol in 20 ml ampoules containing 100 mg. of the

form of nasal or eye drops (1 per cent solution) or incorporated in an ointment containing 1 per cent. of the drug.

The other more recent variants which are proving useful are prednisone and prednisolone These analogues are about four times as potent as cortisone and it is claimed that in addition they possess advantages over the parent substance as therapeutic agents Their salt-retaining and hypertensive properties are certainly less than that of cortisone, though their tendency to exacerbate or reactivate peptic ulcers and to cause psychoses are just as strong if not more so than that of the original substance, while the incidence of other side-effects seems to be very similar.

The dosage of cortisone is a matter for individual adjustment. The disease is usually brought into remission with initial amounts of 100 to 300 mg. daily,

after which the dose is gradually reduced to the minimum maintenance level at which useful, if not complete, control of symptoms can be achieved without producing excessive side-effects. The upper limit of dosage which is unlikely to be accompanied by side-effects cannot be stated: it varies from patient to patient. It may be taken as fairly certain, however, that almost invariably side-effects will ultimately be produced by prolonged treatment with daily dosage exceeding 75 mg.

At the time of writing, the only preparations of the hormones which are available for prescription on form EC 10 under the National Health Service are the tablet and injection of cortisone, and the various preparations of hydrocortisone.

GENERAL PRINCIPLES OF TREATMENT

ætiological agent may persist indefinitely, and a return of signs and symptoms following withdrawal of the hormone almost invariably ensues. This "rebound" phenomenon often occurs in a peculiarly virulent form. In such

physician to decide whether the use of the hormones is justified or not. The decision is not difficult if a patient is desperately ill and death is otherwise certain, or if the inflammatory or allergic reaction is intermittent or self-

hormones being used for their physiological rather than for their pharmacological effects.

THERAPEUTIC USE IN VARIOUS DISEASES

I. TO INDUCE HYPERCORTICISM

Collagen Diseases.—Whatever may be the ætiology of the tissue damage in diseases such as disseminated lupus, polyarteritis, temporal arteritis, dermatomyositis and scleroderma, there is clear evidence that cortisone modifies the tissue reactions in such disorders (see p. 757) Since no other treatment will alter the course of these grave diseases, the same arguments as have been advanced against the routine treatment of rheumatoid arthritis by cortisone

should not be applied to them. Hormonal treatment may be life-saving during the acute episodes and may occasionally tide the patient over his illness until there is a spontaneous remission—an admittedly rare occurrence. Perhaps [illegible] when treatment [illegible]

[illegible] icks of which last only for a matter of weeks and seldom longer than two months, and it is possible to suppress the pyrexia, pain and swelling in the joints and other systemic manifestations throughout the whole course of the attack by hormonal treatment. Such treatment does not, of course, reverse cardiac damage resulting from previous attacks, nor does it prevent recurrences of rheumatic fever. Whether it reduces the frequency of valvular damage is a question that remains to be answered, and some time will elapse before adequate data on this point are available The question even arises as to whether cortisone is more effective than salicylates in suppressing the symptoms of rheumatic fever, and indeed it has been suggested that both operate in the same manner; both alleviate pain and reduce temperature and the erythrocyte sedimentation rate; both increase the excretion of uric acid, raise the blood sugar and lead to fluid retention in [illegible]

[illegible]

Gout.—It is generally agreed that the hormones are effective in relieving the acute episodes of gout, though large doses may be required, and on withdrawing the drug an exceptionally severe attack may occur. As the majority of cases respond satisfactorily to adequate treatment with colchicine and later with aspirin and dietetic restriction, it is probably most unwise to employ hormonal treatment in this disorder (see p 758).

Sarcoidosis.—Sarcoidosis is a granulomatous condition which may be benign and may not significantly affect the health of the patient, in these circumstances no treatment is required. On the other hand, it may be severe [illegible]

improvement can be obtained in a large number of such cases by the use of cortisone, and the same can be said for other pulmonary granulomatoses, such as that caused by beryllium, in which cortisone may prevent or reverse the formation of granulomatous tissue in the early stages before irreversible pulmonary fibrosis and emphysema have developed (see p. 683).

Allergic Diseases.—The nature of the allergic and hypersensitivity responses to the hormones has been mentioned already. The clinical conditions belonging to this group are asthma, hay fever, atopic eczema, exfoliative dermatitis, serum sickness, urticaria, angioneurotic œdema and drug hypersensitivity reactions.

The response of these conditions to cortisone is almost invariably rapid and

use may be life-saving. Lengthy remissions often occur in pemphigus, and once remission has been brought about by hormonal treatment it is probably wise to discontinue it till relapse is once more imminent. In the intervals between periods of treatment the patient is enabled to recover from any side-effects produced by the drug.

Ophthalmological Conditions.—One of the most promising fields for

only of allergic ophthalmic reactions but also those due to bacterial and toxic agents. Administration seems, therefore, to be ideally indicated in acute iritis and iridocyclitis, in which, unless the inflammatory process is promptly checked, serious consequences such as cataract and glaucoma may occur. Many other ophthalmological conditions respond favourably to cortisone, but specialist advice should be obtained prior to its use.

II. REPLACEMENT THERAPY

When cortisone is used as replacement therapy it should be remembered that endogenous adrenocortical output is lacking, and the patient is thereby rendered peculiarly sensitive to stresses and infections. It is therefore important to ensure that once treatment is started it is continued indefinitely, and that supplementary cortisone should be given during any intercurrent illness or infection.

Addison's Disease.—If we could restore functioning adrenal cortical tissue, the patient suffering from Addison's disease could be cured. In theory it might be possible to stimulate the growth of any remaining shreds of adrenal cortex by the administration of corticotrophin. Unfortunately this has proved to be valueless in practice, and we must assume that Addison's disease does not develop until the glands are almost entirely or completely destroyed. It must, therefore, be concluded that Addison's disease is incurable and reliance must be placed entirely on replacement therapy, just as in cases of myxœdema. Fortunately in deoxycortone acetate and cortisone we have two synthetic steroids which enable us to undertake this replacement satisfactorily. The first of these, deoxycortone, is a member of the family of mineralocorticoids and is almost entirely concerned with the regulation of electrolyte metabolism; it has no effect on the deranged carbohydrate and protein metabolism, or on the failure

In the days when only

he outlook for patients

to the hopeless one of th

available, remained very

often of a comparatively trivial description, which precipitated them into Addisonian crisis. Further, a large proportion of the patients maintained on deoxycortone alone were unable to work and very few of them could perform

many of the patients are now fit for strenuous work.

daily doses of from 12·5 mg. to 25 mg. are quite adequate, though in crisis large

doses of intravenous hydrocortisone should be given. Even in the hitherto invariably fatal Waterhouse-Friderichsen syndrome, reports are appearing of survival as the result of cortisone treatment. So successful has cortisone proved in Addison's disease that many believe that injections or implants of deoxycortone are now superfluous and that sole reliance can be placed on oral cortisone. In these circumstances rather larger daily maintenance doses are necessary of from

preferable form of therapy (see p. 372).

Bilateral Adrenalectomy.—Since the introduction of potent replacement therapy bilateral adrenalectomy has become a practical procedure for patients suffering from metastatic cancer of the breast or prostate or from malignant hypertension. Two hundred milligrammes of cortisone are given on the day previous to operation

after, dropping to 1c

clinical condition of t

to the same considerations as in the maintenance treatment of Addison's disease (see p. 372).

Adrenal Hyperplasia.—As has been indicated, cortisone powerfully inhibits adreno-cortical function, probably by suppressing the release of corticotrophin by the pituitary. It is thus of value in congenital adrenal hyperplasia or female pseudo-hermaphrodism in which the clinical manifestations of virilism can be reversed, though the treatment will probably have to be maintained permanently. The dose is determined by finding the minimal effective one which will keep the 17-ketosteroid excretion below 8 mg. per twenty-four hours. It is usual after the initial suppressive treatment for this to be accom-

pituitarism as the result of permanent treatment by corticotrophin or cortisone, patients who may have been in a practically dormant hibernating condition for years being converted into relatively normal human beings. Theoretically corticotrophin would seem to be the hormone of choice in hypopituitarism, and there is no doubt that by its administration an adrenal cortex, even when it has lain dormant for many years, may be stimulated once more into active life; it is also our impression that on the whole patients maintained on injections of corticotrophin are a little better than patients maintained on cortisone. Nevertheless, in practice the difference in effect produced by the two hormones is very slight—much less than might be expected—and many patients feel that the advantage of the convenience of oral cortisone greatly outweighs the slightly superior clinical effects produced by injected corticotrophin. Dosage is still a matter for some speculation, though it conforms with the principle that, where there is lack of endogenous hormone, much smaller amounts are required to replace it than when exogenously administered extract is supplementary to normal endogenous production. If cortisone is used, the dose approximates to that required in Addison's disease; with corticotrophin, 30 mg. of the gel injected twice a week is usually sufficient (see p. 377).

D. M. DUNLOP.

ANTICOAGULANT THERAPY.

ONE OF THE STRIKING DEVELOPMENTS in therapeutics in the last ten years is the introduction of anticoagulant therapy, now used in a great variety of conditions *characterized by intravascular* clotting, both arterial and venous. Besides abnormalities in the clotting mechanism, other factors such as venous stasis, prolonged immobilization and pathological changes in vessel walls call for consideration. At present the most promising line of treatment in many cases is the use of anticoagulant drugs, provided this is adequately controlled

The anticoagulants in common use fall into two main groups, distinct in respect of chemistry, mode of action, administration and methods of control: they are (1) heparin and its analogues and (2) the coumarin derivatives.

Heparin and its Analogues.—These are all polysaccharides of high molecular weight. Heparin is a naturally occurring anticoagulant which comes from mast cells Its most important action is to inactivate thrombin with immediate prolongation of the blood clotting time—an effect which lasts for three to six hours after a single dose. Heparin is relatively safe even when given

ately heparin is effective only when given parenterally, and the method most used in Britain is intermittent intravenous injections of 10,000 International Units every six hours, the aim being to keep the blood clotting time twice to three times that of the control With this regimen, wide fluctuations in clotting time occur, *but in practice the method has been found satisfactory in the great* majority of patients, and laboratory estimates of the clotting time are unnecessary. Intramuscular injections of heparin are less certain in effect than when it is

are not very satisfactory.

Intravenous heparin is the most certain and effective anticoagulant, and should always be used initially when there is an urgent indication for treatment. Long-continued administration is unnecessary and undesirable, because of the expense of the drug and the necessity for its intravenous *injection, and treatment* can be continued with one of the coumarin drugs. Dangerous bleeding is rare,
... the first sign. If it is alarming, a blood
te should
1. These

Other substances with the same action as heparin, but cheaper and easier to prepare, are at present under trial in this country Dextran sulphate is the most promising of these synthetic analogues of heparin. It has the same properties as heparin except that the response to an intravenous dose of dextran sulphate of equivalent weight lasts a few hours longer. Intravenous injection

of 5,000 I.U. six-hourly is satisfactory in most cases, while in others good results have been obtained with 5,000 I.U. twice daily. In preliminary tests no toxic effects have occurred, but more extensive trials are necessary.

Coumarin Anticoagulants.—At present the best drugs for routine use are ethyl biscoumacetate (Tromexan) and phenindione (Dindevan). Ethyl biscoumacetate is most effective when given in dosage of 300 mg every six hours until the one-stage " prothrombin " test, performed daily, is in the therapeutic range. This is reached in twenty-four to thirty-six hours, the total

[illegible]

majority of cases in twenty-four to forty-eight hours. Maintenance doses vary less than with ethyl biscoumacetate and range from 50 to 150 mg daily, usually given as a single dose. An even control of the " prothrombin " level is easily achieved with phenindione, and as the return of the prothrombin time to normal on cessation of treatment is as rapid as with ethyl biscoumacetate (twenty-four to forty-eight hours), phenindione must be considered the drug of choice for coumarin therapy.

[illegible]

now known that at least two factors concerned in thromboplastin generation are affected by the administration of these drugs, namely the Christmas factor (factor IX) and factor X Factor VII, which is profoundly depressed by coumarin anticoagulants, is not concerned with thromboplastin generation even though this is the basis of the prothrombin test which has proved to be satisfactory in the control of treatment Blood prothrombin may also be affected by the [illegible] intimately associated [illegible]aled by the one-stage

Control of Therapy.—It is the usual practice to control therapy with coumarin anticoagulant drugs by estimating the one-stage " prothrombin " [illegible] control level Daily examinations are required until the therapeutic level is reached Thereafter the prothrombin time must be estimated daily for a further ten days or a fortnight to assess the maintenance dose required for that particular patient. It is customary to express the result either in seconds or as " percentage prothrombin " read from a calibration curve prepared from samples of normal plasma, the prothrombin concentrations of which have been reduced by saline dilution A range of 10 to 30 per cent. of normal on the dilution curve is now [illegible]

[illegible]r of years ago long-term out[illegible]ible risks, recent experience in [illegible] that it is possible to maintain patients on anticoagulants for long periods in a satisfactory manner. The

prothrombin time should be estimated every two to four weeks, and it is essential in the organization of such a clinic that one physician be responsible for therapy, and that the general practitioner in charge of the case at home should be fully conversant with the possible complications and difficulties that may be encountered

Out-patient anticoagulant therapy must be stopped when any surgical procedure has to be carried out, including dental extraction. The patient should therefore carry with him a card stating that he is on anticoagulant therapy, giving his blood group and the address and telephone number of the clinic which is supervising his treatment. When emergency surgical procedures have to be carried out within an hour or two, the best treatment is the intravenous transfusion of fresh blood, and this will allow the operation to be undertaken with safety. If longer delay is possible, then the oral administration of 20 mg. of vitamin K_1 will produce a satisfactory state of affairs for operative work within six to eight hours A preparation of vitamin K_1 is available which is suitable for intravenous administration, but it has no advantage over the oral preparation unless severe vomiting is present.

Therapy has also to be stopped when a cerebral thrombosis or embolism occurs, because hæmorrhage into the infarcted area of the brain may result, [illegible] Under these circum-

[illegible]

The development of cardiac failure with hepatic congestion may make control of anticoagulant therapy more difficult because of derangement of liver function, and if signs of failure persist in spite of adequate treatment with digitalis and mersalyl, anticoagulant therapy should not be continued except in hospital.

The initial hæmorrhage which may result from coumarin therapy usually occurs from the urinary tract. When the initial hæmorrhage takes place in other situations, this strongly suggests the presence of a co-existing lesion which may bleed, such as a peptic or carcinomatous ulcer or a tuberculous focus. All that is required in the majority of cases developing a mild hæmaturia is to stop the administration of the drug. In the more severe cases the administration of a preparation of vitamin K is indicated, and sometimes a transfusion of fresh blood is also required

Of all the vitamin K preparations which have been studied by the writer, the emulsion of vitamin K_1 (Roche) given by mouth has proved to be the most satisfactory, and the dosage required is only in the region of 10 to 50 mg. daily, [illegible] Though vitamin K_1 can be given parenter-
[illegible] oute remains the one

[illegible] he contra-indications
[illegible] llows :

(1) Any hæmorrhagic tendency, whether from primary disease of the blood or blood vessels such as hæmophilia and purpura, or from vitamin C or vitamin [illegible] and the consequent

[illegible]

patients with hepatic cirrhosis.

(2) Ulcers, benign or malignant, in any site, but particularly in the alimentary

and urinary tracts. Recent gastric or duodenal ulceration makes anticoagulant therapy very hazardous

(3) Recent trauma to the brain or spinal cord. Destructive hæmorrhage from anticoagulants is especially likely in such lesions, which include recent cerebral embolism or thrombosis. [illegible] whose cerebral embolus is only c[illegible] episodes presents a difficult proble[illegible] coagulants has to be weighed against the probable prevention or reduction in number of further embolic incidents resulting from their use. It is best to compromise by withholding anticoagulants for the first ten to fourteen days after the cerebral lesions and then, if recovery is good, to start cautious treatment with [illegible]

[illegible] coagulants is increased by accumulation in the body, making great caution necessary in their use.

(6) Pregnancy

R. B. Hunter

prothrombin time should be estimated every two to four weeks, and it is essential in the organization of such a clinic that one physician be responsible for therapy, and that the general practitioner in charge of the case at home should be fully conversant with the possible complications and difficulties that may be encountered.

Out-patient anticoagulant therapy must be stopped when any surgical procedure has to be carried out, including dental extraction. The patient

carried out within an hour or two, the best treatment is the intravenous transfusion of fresh blood, and this will allow the operation to be undertaken with safety. If longer delay is possible, then the oral administration of 20 mg. of vitamin K_1 will produce a satisfactory state of affairs for operative work within six to eight hours A preparation of vitamin K_1 is available which is suitable for intravenous administration, but it has no advantage over the oral preparation unless severe vomiting is present.

Therapy has also to be stopped when a cerebral thrombosis or embolism occurs, because hæmorrhage into the infarcted area of the brain may result, causing the death of the patient within a matter of hours. Under these circumstances vitamin K_1 (20 mg. by mouth or intravenously) should be administered as soon as possible.

The development of cardiac failure with hepatic congestion may make control of anticoagulant therapy more difficult because of derangement of liver function, and if signs of failure persist in spite of adequate treatment with digitalis and mersalyl, anticoagulant therapy should not be continued except in hospital

The initial hæmorrhage which may result from coumarin therapy usually occurs from the urinary tract. When the initial hæmorrhage takes place in other situations, this strongly suggests the presence of a co-existing lesion which may bleed, such as a peptic or carcinomatous ulcer or a tuberculous focus. All that is required in the majority of cases developing a mild hæmaturia is to stop the administration of the drug. In the more severe cases the administration of a preparation of vitamin K is indicated, and sometimes a transfusion of fresh blood is also required

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daily,

nter-

one

patients with hepatic cirrhosis.

(2) Ulcers, benign or malignant, in any site, but particularly in the alimentary

and urinary tracts. Recent gastric or duodenal ulceration makes anticoagulant therapy very hazardous.

(3) Recent trauma to the brain or spinal cord. Destructive hæmorrhage from anticoagulants is especially likely in such lesions, which include recent cerebral embolism or thrombosis. The young patient with auricular fibrillation and a cerebral embolus is only one in a life-threatening series of embolic [illegible] problem in which the possible danger of anti- [illegible] reduction in [illegible] is best to com- [illegible] een days after [illegible] treatment with promise by withholding [illegible] the cerebral lesions and then, if recovery is good, to sta[illegible]

[illegible] Here there is said to be a danger of [illegible] do badly with anticoagulants.

(5) Severe renal insufficiency, in which the poten[illegible] coagulants is increased by accumulation in the body, making great caution necessary in their use

(6) Pregnancy.

R B Hunter.

DEHYDRATION, ELECTROLYTE DEFICIENCIES AND DISTURBANCES OF ACID-BASE EQUILIBRIUM

REDUCTION IN THE FLUID content of the body can arise from a variety of causes—deficient intake or excessive loss of water or electrolytes, both extracellular and intracellular, or disturbances of the acid-base equilibrium of the body fluids. These syndromes differ not only in the [illegible]

is to be given for each.

ANATOMY AND PHYSIOLOGY OF THE BODY FLUIDS

Besides differing in anatomical situation, the extracellular fluid (plasma and interstitial fluid) and intracellular fluid differ also in chemical composition. The two compartments of extracellular fluid are separated from each other by the capillary walls, which are freely permeable to all of the plasma constituents except protein. The electrolyte composition of both is therefore essentially the same; the osmotically important ions being the cation sodium, comprising about 90 per cent. of the total cations of extracellular fluid, and the anions [illegible]

[illegible] id by the cell [illegible] that the chief cation of intracellular fluid is potassium, with a lesser amount of magnesium and only about one-twentieth as much sodium as in extracellular fluid, while the chief anions are phosphate and protein, with a lesser amount of bicarbonate. This great disparity in chemical composition between the two fluids is not maintained, as was formerly believed, by an impermeability of the cell wall to the passage of ions across it. On the contrary, the cell wall is now known to be permeable to sodium and potassium ions particularly, and the differing concentrations of these two ions on either side of the cell wall are brought about by active metabolic processes within the cell, requiring energy expenditure.

Clinical significance attaches to this new concept, in that in disturbances of electrolyte metabolism, not only water but also sodium and potassium and other ions move across the cell membrane. We must therefore now think of body fluid depletion as involving not only demonstrable changes in the composition of extracellular fluid but also alterations in intracellular electrolytes and disturbance of the acid-base equilibrium within the cells. Therapy must be planned to correct intracellular as well as extracellular electrolyte disturbances. Measures directed solely to the latter purpose may be ineffective and even harmful, unless the disturbance of intracellular electrolyte composition is treated at the same time.

Control of the volume of the body fluids is apparently of less vital significance to the body than maintenance of osmotic tonicity. Therefore the volume of

[illegible]

(of which the most important osmotically are sodium and potassium), since some of the anions are formed in metabolism. Control of the amount of sodium and potassium in the body is vested in the kidneys, which perform this function by variation in the reabsorption of sodium and potassium in the distal tubules according to the need of the body for retention or excretion of [illegible]

pituitary, which controls the amount of water reabsorbed in the distal tubules

Although the body is entirely dependent on the food for its supply of inorganic cations, the efficiency of the renal mechanism for their conservation in healthy people is such that a clinically important degree of depletion will not occur even on a virtually salt-free diet, and requires for its development some abnormal loss of sodium or potassium from the body.

On the other hand, the maintenance of water balance requires a constant supply of water to make good the unavoidable water losses of the body in [illegible]

secretion , these processes are part of the heat-loss mechanism and cannot be altered in response to the body's need for water By the obligatory urine secretion is meant the minimal amount of water required to rid the body of waste products at the maximal concentrating power of the kidneys. The volume depends on the amount of waste products to be excreted and on the concentrating power of the kidneys ; in a healthy adult, it is in the region of 500 ml per day

Except in diarrhœa, only a little water, about 100 to 200 ml. daily, is lost in the fæces

Therefore a total daily unavoidable water loss of at least 1,500 ml. in an adult (and more if there is a significant amount of sweat secretion) must be met by water intake if the body's water content is to be maintained. Any excess of intake over this figure is excreted in the urine. Water is added to the body not only by taking fluid as such but also as the water content of solid foods and " metabolic " water produced in the oxidation of foodstuffs.

THE PATHOGENESIS OF DEHYDRATION

A very important advance in our understanding of the mechanisms underlying dehydration has been the recognition that reduction in body fluid can arise in two ways, through shortage of water alone or through loss of electrolytes While either form can readily be produced experimentally, in clinical practice the conditions leading to dehydration most often involve both a reduction in water intake and an abnormal salt loss, so that a third or mixed type of dehydration is most commonly encountered Nevertheless, it will help in an understanding of the treatment of dehydration in general if the pathogenesis of " pure " water depletion and " pure " salt depletion is each considered separately.

The clinical diagnosis of these disorders presents peculiar difficulties in that they are rarely accompanied by pathognomonic symptoms or signs. Hence it has been thought wise to preface each section with a note of the clinical conditions likely to be attended by them. Accurate diagnosis is largely based upon knowing the diseases and circumstances in which the disorders are likely to exist and confirming this suspicion with appropriate physical examination and chemical investigations.

Water Depletion (*Primary Dehydration or Sodium Excess without Water Excess*).—This condition arises when the unavoidable water losses are not met from ingested water or water formed in metabolism Thanks to the safeguard [illegible]

or in those who are comatose from any cause or so apathetic and weak, as is common for example in the aged, that they fail to respond to the stimulus of thirst To meet the inescapable water demands, water is drawn first from the extracellular fluid, which therefore becomes hypertonic in relation to the cell fluid Osmotic equilibrium is re-established by the passage of water out of the cells into the extracellular fluid. The water loss is shared by the extracellular and intracellular fluids in proportion to the relative size of the two compartments ; the bulk of the water loss thus falls on the cell fluid, and the volume of extracellular fluid (including the blood) is therefore not greatly diminished. As a result, renal function is not seriously impaired, but the limitation of available water for urine formation prevents the complete excretion of urea and electrolytes even at the maximal concentrating power of the kidneys.

The blood urea and plasma sodium therefore increase slowly—indeed the essential biochemical feature of this syndrome is an increase in the concentration of sodium in the extracellular fluid But it is important to realize that the syndrome of water depletion can arise even when the sodium content of the body is lower than normal, under conditions where the rate of water loss outstrips that of sodium A raised plasma sodium therefore does not exclude sodium deficit in the body, but shows that the water deficit is even greater and therefore should have priority in treatment.

The two cardinal features of water depletion are severe thirst, caused by the increased osmolarity of the body fluids, and a reduction in the urine volume to a figure representing the obligatory urine secretion. If water depletion continues, increasing weakness and mental confusion occur, and the condition ends in collapse and death when the body-weight has fallen by about 15 per cent.

Salt Depletion (*Secondary Dehydration*).—As we have seen, the development of a salt depletion state only arises when there is some abnormal loss of sodium from the body, which may occur in excessive sweating, in loss of alimentary secretions through vomiting, diarrhœa or suction drainage of gastric or intestinal contents, or excessive excretion of sodium in the urine The latter channel of loss is not so obvious as the other two, but can lead to sodium depletion in one of two ways : (1) defective reabsorption of sodium in the renal tubules (from lack of adrenal hormones, damage to tubules in renal disease, or because of interference with sodium reabsorption through the

to either acidosis or alkalosis Sodium depletion from any of the above causes will of course involve the loss of equivalent amounts of water as part of the process

cellular field inhibits pituitary antidiuretic hormone secretion and the resulting water diuresis lessens extracellular fluid volume but tends to restore its sodium ... m the

ration

fluids in a patient with salt depletion or suppression of urine may so increase the water content of the cells as to lead to the dangerous and even fatal condition of water intoxication.

At the onset of salt depletion, the compensatory reduction in extracellular water that occurs may be sufficient to maintain a normal sodium concentration in extracellular fluid, but if salt loss continues, osmotic standards have to be relaxed in an attempt to maintain plasma volume, and the sodium concentration in extracellular fluid accordingly begins to fall

The major functional disturbances of salt depletion can be attributed to the decrease in plasma volume and the increase in the viscosity of the blood. The

loss of interstitial fluid as indicated by the characteristic signs of dehydration.

fluid intake is not restricted In the final stages of oligæmic shock, however, anuria may supervene when the blood pressure falls below the critical level for maintenance of glomerular filtration.

In contradistinction to water depletion, evidence of reduced plasma volume is afforded by rising hæmatocrit, hæmoglobin and plasma protein values The blood urea rises more rapidly than in pure water depletion owing to the diminished glomerular filtration Except in early or mild salt depletion the plasma sodium level is reduced, and renal conservation of this ion causes

of salt depletion. But unfortunately it is not infallible, since in salt depletion due to adrenal insufficiency, " salt-losing " nephritis or acidosis, sodium and with it chloride is still present in the urine

Mixed Water and Salt Depletion.—In clinical practice experience shows that it is very uncommon for sodium depletion to occur without being attended by abnormal loss of water. The conditions giving rise to mixed water and salt

depletion are those described under pure salt depletion in which the intake of water is reduced or is insufficient to balance the loss.

Under such conditions, water loss outstrips sodium loss because of the unavoidable loss of water *unaccompanied by sodium through the skin and* lungs. The reduction in the water content of the body is therefore greater than that resulting from a corresponding degree of "pure" salt depletion, and the extracellular fluid, though diminished in volume, tends to be hypertonic despite the reduction in the salt content of the body as a whole; this leads to some withdrawal of water from the cells.

The clinical and laboratory manifestations of mixed water and salt depletion are therefore a combination of the salient features of the "pure" water and salt depletion states. Patients will show the peripheral circulatory failure and subcutaneous dehydration due to reduction of extracellular fluid volume, but will also have oliguria and suffer from the thirst arising from hypertonicity of body fluid. *There will be laboratory evidence of hæmoconcentration and the* blood urea will rise rapidly, but the plasma sodium may remain normal or even rise.

Disturbances of Acid-Base Equilibrium in Dehydration.—The disturbances of acid-base equilibrium that are so frequently encountered in association with salt-depletion states may either be primary in the sense that renal adjustment to acidosis or alkalosis has led to depletion of cations and with them water from the body, or may be secondary to a disproportion in the amounts of sodium and chloride ions lost with body fluids.

Metabolic acidosis will be primary in this sense where it is due either to excessive administration of acids or acid-forming salts (e.g. ammonium chloride), to the excessive production of acid metabolites (as in diabetic ketosis), or to a failure of the acid-excretion mechanisms of the kidney (as in renal failure or in renal tubular insufficiency). These conditions all lead to increased excretion in the urine of sodium and potassium ions in combination with anions, with which is excreted a corresponding amount of water. Similarly, renal adjustment to the metabolic alkalosis caused by ingestion of excessive amounts *of soluble alkali involves the increased excretion in the urine of base (bicar-*

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of alkaline sodium bicarbonate in small intestinal contents through diarrhœa, suction or fistulæ, or in the fixation of sodium and the release of hydrogen ions in the gut by ion-exchange resins), acidosis is likely to occur. On the other hand, if chloride is lost in excess of sodium (loss of gastric juice in vomiting or ... the tendency is towards alkalosis Any impairment of

balance.

Apart from the deleterious effects that such disturbances of acid-base

to correct the abnormalities of the body electrolyte pattern caused by acidosis or alkalosis; brief consideration of these abnormalities is therefore necessary In the initial stages of acidosis, fixed base, both sodium from extracellular fluid and potassium from intracellular fluid, is utilized for the neutralization of the excess acid to be excreted by the kidney If the kidneys are healthy, their base-conserving mechanisms (increased titratable acidity of the urine and increased ammonia production) come into play in a few days. But in severe acidosis or where renal function is impaired, as it is so frequently in dehydration, these base-conserving mechanisms are not fully compensatory. Increased amounts of sodium and potassium therefore continue to be excreted in the urine, aggravating any loss of these electrolytes through other channels, and bringing about a depletion of available base, and presumably also an acidosis, within the cells as well as in the extracellular fluid.

The position is more complicated in alkalosis, in that the same parallelism between the alterations in the reaction of the extracellular and intracellular fluid apparently does not hold as it does in acidosis, and the characteristic abnormality of extracellular fluid pattern (hypochloræmia, with a reciprocal

body's cation content and an intracellular acidosis, for the following reasons. The renal tubu'

exchange for tl

alkalosis, loss c

for this purpose, and the tubules therefore have to excrete more potassium ions instead This leads to depletion of potassium within the cells, the place of which is taken by a movement of both sodium and hydrogen ions from extracellular fluid into the cells Thus, the hydrogen ion concentration of the extracellular fluid is further reduced, but that of the cells is increased (intracellular acidosis) Indeed, this migration of hydrogen ions into the cells in partial replacement of potassium seems to be the major factor in perpetuating the extracellular alkalosis, and explains why alkalosis is often difficult to treat unless attention is given to correction of the intracellular potassium depletion.

Renal readjustment to extracellular alkalosis is to excrete increased amounts of base in the form of sodium bicarbonate, but this process aggravates any sodium depletion that has occurred owing to vomiting The loss of both extracellular sodium and intracellular potassium ions involves the loss of corresponding amounts of water and explains the dehydration that arises in alkalosis.

Potassium Depletion in Dehydration.—As we have seen, loss of body water and extracellular electrolytes cause shifts not only in the water but also in the electrolytes of intracellular fluid, particularly potassium. That disturbances of intracellular electrolyte pattern play a major role in producing the manifestations of the various dehydration syndromes is exemplified by the

The control of potassium excretion by the kidney is not so delicate or rapid a process as that dealing with sodium and is more easily disturbed in disease. Nevertheless, it is sufficiently active in health to prevent a reduction in the potassium intake from causing any significant degree of depletion. As in the case of sodium, depletion requires some abnormal loss of potassium, such as may occur either in alimentary secretions or in the urine.

Although alimentary secretions contain more sodium than potassium, *vomiting or diarrhœa can lead to over-all losses of potassium of the same order* as those of sodium, because the resulting dehydration leads to a breakdown in the renal conservation of potassium

The causes of excessive potassium excretion in the urine can be divided ...ses—increased ... chronic renal ... ncern us here. ... *urine include* both water and salt depletion, particularly when there is an associated disturbance of acid-base equilibrium In water depletion, potassium, accompanied by water, passes from the cells into the extracellular fluid, from which the potassium is excreted into the urine—this seems to be part of the physiological mechanism for maintaining extracellular fluid volume when it is threatened by water lack. ... excretion of ... turbances of ... potassium depletion, such as is seen in increased adrenocortical activity or potassium-losing nephritis, tends to produce an alkalosis of the extracellular fluid, *presumably because of migration of hydrogen ions into the cells in* partial replacement of the lost potassium Therefore, as in alkalosis from other causes, the potassium depletion within the cells seems to be associated with acidosis therein.

The potassium ion has important pharmacological actions—on muscular contraction and neural transmission—in addition to its osmotic effect. Reduction of the concentration of potassium in extracellular fluid leads to weakness of skeletal muscles progressing to frank paralysis, and irregularity of heart action which may end in cardiac failure and death from cardiac arrest. Definite clinical manifestations of the disturbed cell functions resulting from intracellular potassium deficiency have not yet been identified, and the only symptom so far attributed to such depletion is atony of the bowel muscle, leading to paralytic ileus.

Thanks to the relatively great bulk of the intracellular potassium and the shifts that can occur from cells to extracellular fluid, it requires a major depletion of the body *potassium before its concentration in extracellular fluid falls to a* level that produces the severe symptoms mentioned above. But a significant hypopotassæmia can exist without producing any but vague symptoms such as weakness, irritability, muscular hyperalgesia and abdominal distension, and there are no means of predicting whether or not *persistence of hypopotassæmia* will precipitate the more serious manifestations of potassium depletion.

It is therefore a wise precaution to suspect and be prepared to treat potassium depletion in any dehydrated patient. The clinical diagnosis of potassium depletion is a difficult problem, however, and must depend largely on an appreciation of the conditions that can bring it about, a search for symptoms

that fail to respond to conventional salt and fluid therapy, and the employment of such laboratory tests as may be of value. It is unfortunate from the latter point of view that the bulk of the body potassium is within the cells and hence inaccessible for analytical purposes. The finding of a subnormal serum potassium certainly points to a depletion of the body stores, but the serum level may be normal or even elevated in the presence of a significant potassium depletion when renal function is impaired either by primary kidney disease or from extrarenal causes such as salt depletion

The only intracellular fluid readily accessible for analysis is that within the erythrocytes, and determination of the erythrocyte potassium concentration (an easy procedure if a flame photometer is available) has been suggested as an index of the state of the general intracellular stores of potassium. Opinion varies as to the validity of this assumption, but practical experience has shown that a low erythrocyte potassium concentration is a characteristic finding in the more chronic or advanced depletion states, and betokens a more severe deficiency, requiring more potassium for its correction, than when only the extracellular (serum) potassium is low.

Treatment of dehydration with fluids designed only to restore extracellular electrolytes may not only be ineffective but also dangerous if potassium depletion is present. The latter is aggravated by dilution of extracellular fluid with the infused potassium-free fluids, also, sodium ions from the infusion fluid will enter the cells in replacement of the depleted potassium content therein; experimentally, this has been shown to precipitate the myocardial necrosis of potassium depletion.

TREATMENT OF DEHYDRATION

PROPHYLAXIS

Enough has been said about the [illegible]

[illegible]

seen, the minimal water intake necessary to cover the various obligatory water losses is about 1 5 litres daily in health, but obviously may be much greater where there is abnormal water loss in sweat or alimentary secretions or where the [illegible]

[illegible]

1 litre and preferably should be in the region of 1 5 litres per twenty-four [illegible]

[illegible]

It is even less easy to lay down any arbitrary figures for the amount of salt

required. Where there is no abnormal salt loss, equilibrium can be maintained on very small salt intakes of less than 1 to 2 g. daily. But except where salt restriction is being carried out as a deliberate therapeutic policy, as in cases with œdema, it is unwise to allow the salt intake to be limited to such low figures, and at least 5 g of salt should be given daily. If the patient is able to eat cooked meals, the salt used in cooking or added at table will meet this figure; where a fluid diet is being given, the salt may be included in soup, meat extract drinks or tomato juice, or beverages such as fruit cordials and tea can be made with 0·2 per cent. saline instead of plain water. Where abnormal salt loss develops during the course of an illness, the salt intake must be correspondingly increased and the treatment then becomes that of salt depletion discussed below. All that need be said here is that determination of the urinary chloride concentration provides a useful indication of the adequacy of the salt intake. The aim in adults should be a urinary sodium chloride concentration of 3 to 5 g per litre.

Wherever possible, the requisite amounts of water and salt to meet these criteria should be given by mouth When the patient's condition precludes this, water and salt must be given as a continuous drip either by gavage in conscious patients (i.e. through a Ryle's tube introduced into the stomach via the mouth or nose) or parenterally by the subcutaneous, or preferably the intravenous route. It is obvious that the total daily fluid requirement of 2·5 litres or more per day must not be supplied exclusively as isotonic saline (containing 8·5 g. of sodium chloride per litre) to a patient who is not suffering from salt depletion. Not more than one litre should be given as saline and the remainder of the fluid intake should be in the form of 5 per cent. glucose solution. If, however, fluid is introduced by gavage, hypotonic saline can be used and by this means adequate fluid can be given without excessive salt.

TREATMENT OF ESTABLISHED DEHYDRATION

From what has been said regarding the mechanism leading to dehydration in water and salt depletion respectively, it is clear that the treatment required for each type is radically different. In water depletion, the need is to reduce the hypertonicity of the body fluids by restoring their water content to normal, whereas in salt depletion the urgent need is to correct the deficit in the electrolytes of the body fluids and so cause expansion of the reduced extracellular fluid volume. It must be emphasized that the wrong treatment applied to either type of depletion will not only fail to relieve the dehydration but may even aggravate the patient's condition. Thus if saline is administered to a

tonicity of extracellular fluid or, where kidney function is impaired, will pass into the cells and tend to produce the dangerous condition of water intoxication

The first essential, therefore, in the treatment of dehydration is to arrive at a diagnosis as to which of the three types is present, from the history and the distinguishing clinical manifestations and laboratory findings mentioned in discussing the pathogenesis of dehydration.

In all three forms of dehydration the essentials of practical treatment are

summed up in the answers to three questions: (1) What fluid should be given? (2) How much of this fluid should be given? and (3) By what route and at what rate should the fluid be administered?

Water Depletion.—The fluid required is of course water, given by mouth if the patient can drink it, otherwise by gavage or as isotonic (5 per cent) glucose solution intravenously.

There are no simple laboratory procedures that help in assessing the extent

severity of water depletion, viz:

Mild—Thirst and oliguria as the only symptoms. Water deficit about 2 per cent. of the body weight (i e. about 1 5 litres or 3 pints in the "average" man of 70 kg or 11 stones).

Moderate.—Weakness and some mental confusion added to the above clinical manifestations. Water deficit about 6 per cent. of the body-weight (i.e. about 4 litres or 7 pints in the adult).

Severe—Great physical prostration and mental confusion apparent. Water deficit 7 to 14 per cent. of the body-weight (i e. 5 to 10 litres or 9 to 18 pints in the adult).

In assessing the amount of water to be given, one must of course add to the estimated water deficit the current minimal daily water loss of at least 1 5 litres. This means that even the mildest case of water depletion will need at least 3 litres in the first twenty-four hours

The rate of administration will depend on the state of the patient. Pure water depletion does not demand such heroic measures of rapid intravenous infusion as are required in the circulatory failure of salt depletion Restoration

the measurement of the urine volume. The aim should be the restoration of the urine volume to about 500 ml. every eight hours, a level that is indicative of relief of the water deficit except in cases of renal disease where, as already mentioned, a urine volume of about 800 ml every eight hours is desirable.

Salt Depletion.—The immediate aim of treatment is restoration of the extracellular fluid volume as rapidly as is safe without overburdening the heart; this will restore such vital functions as blood volume and pressure, renal circulation and urinary output and tissue oxygenation by relieving the oligæmic circulatory failure which is the threat to life in salt depletion Second only in importance to this are measures to correct depletion of intracellular electrolytes, particularly potassium, and to restore the *p*H of the extracellular fluid to normal if acidosis or alkalosis are present

The initial fluid of choice is therefore isotonic saline. In patients where the circulatory failure is severe enough to have produced marked oliguria, fluids such as blood, plasma or solutions for correction of potassium depletion or abnormalities of *p*H are best withheld until saline infusion has produced a satisfactory urine output

It must be admitted that the quantity of electrolytes required to restore a salt-depleted patient to normal cannot be estimated with precision from any

required. Where there is no abnormal salt loss, equilibrium can be maintained on very small salt intakes of less than 1 to 2 g. daily. But except where salt restriction is being carried out as a deliberate therapeutic policy, as in cases with œdema, it is unwise to allow the salt intake to be limited to such low figures, and at least 5 g of salt should be given daily. If the patient is able to eat cooked meals, the salt used in cooking or added at table will meet this figure; where a fluid diet is being given, the salt may be included in soup, meat extract drinks or tomato juice, or beverages such as fruit cordials and tea can be made with 0·2 per cent. saline instead of plain water. Where abnormal [illegible]

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luid volume deficit in terms of litres of isotonic saline is determined from the ormula:

$$\frac{600\text{—true plasma or serum chloride as mg. NaCl per 100 ml.}}{25} = \text{deficit in litres of isotonic saline.}$$

To the estimate [illegible] isotonic saline required to make g[illegible] be added the fluid and salt to co[illegible]piration, urine output and any continuing loss of body fluids. The first two will need the administration of about 2 litres of water daily (as 5 per cent. glucose intraven- [illegible]

be improved. At the same time, the rate of infusion must not be so rapid as to overburden the heart, and it is probably unwise to give more than 5 litres of saline intravenously per twenty-four hours, plus the recommended amount of glucose solution if the patient cannot drink

In severe salt depletion, the extent of the deficit may be forbiddingly large —of the order of up to 10 litres as isotonic saline It is obviously impossible to repair such a severe reduction of extracellular fluid volume within twenty-four hours, and two or even three days may have to be allowed. Such slowness of repair can be accepted unless the peripheral circulatory failure is extreme and renal blood flow has fallen to the extent of producing anuria In such patients the rapid introduction of large amounts of fluid by vein is inadvisable, yet there is an urgent need for sufficient sodium to permit restoration of blood volume and renal blood flow A case exists here for the use of hypertonic (double-strength i.e. 1 7 per cent) saline, which permits the sodium deficit to be met with only half the volume of fluid The remainder of the water required to dilute the hypertonic saline to normal tonicity will be withdrawn from the overhydrated cells. But since there are no means of assessing the extent of cellular overhydration, it is wise to restrict the use of hypertonic saline to patients who can take water by mouth

Special measures are necessary where salt depletion is accompanied by a *significant disturbance of acid-base balance, as discussed below. But it must be* realized that even where the alkali reserve is normal, the infusion of large amounts of isotonic saline will tend to cause acidosis, since saline contains no bicarbonate and therefore has an excess of fixed acid ions of about 30 milli-equivalents per litre as compared with extracellular fluid. If, as is so common in salt depletion, renal function is impaired by inadequate circulation, the kidneys may not be able to excrete the excess chloride ions, and acidosis, which may be clinically important in an already severely ill patient, results. The development of this so-called " dilution acidosis " can be prevented by the infusion of 1 litre of isotonic (1/6 molar, or 1 87 per cent.) sodium lactate solution for every 4 litres of isotonic saline. Sterile sodium lactate solution is supplied by the manufacturers in ampoules or bottles containing 40 ml of molar strength —dilution of one such ampoule with 200 ml of water or 5 per cent glucose

laboratory tests, and the best that can be accomplished initially is a provisional assessment that will serve as a general guide to the amount of saline likely to be required. An approximate estimate of the extent of the extracellular salt and water loss can be obtained from the clinical history and clinical examination. A mild degree of salt and water depletion up to the equivalent of about 2 litres isotonic saline can occur without detectable evidence of dehydration or significant alteration in blood pressure or pulse rate. Its existence may however be suspected from the history of fluid loss and food consumed. If signs of dehydration are obvious and the blood pressure is moderately reduced, the salt and water deficit will be equivalent to 4 to 6 litres (7 to 11 pints); while severe clinical manifestations with circulatory failure and a systolic blood pressure below 90 mm. Hg indicate a salt and water deficit equivalent to 6 to 10 litres (11 to 18 pints).

Among laboratory procedures, only determination of the serum sodium concentration provides some sort of quantitative assessment of the extent of the extracellular fluid depletion; with the introduction of the flame photometer, this analysis is simple and rapid. Black has devised a formula from which the extent of the sodium deficiency can be calculated in terms of litres of isotonic saline from the serum sodium concentration expressed as milli-equivalents per litre, viz.:

$$\frac{140-(\text{observed serum sodium})}{3{\cdot}5} = \text{sodium deficit in litres of isotonic saline.}$$

(NOTE.—Although sodium is largely confined to the extracellular fluid, total body water volume has been used in the construction of this formula, for two reasons Firstly, the shift [illegible]
depletion keeps the extracellular [illegible]
figure that truly reflects the exte[illegible]
" volume of distribution " of injected sodium approximates nearly to the total body water volume.)

It cannot be emphasized too strongly here that the mere demonstration of a low serum sodium should never be made the basis for saline therapy. In [illegible] lead to sodium [illegible] sodium may [illegible] depletion of body sodium and no shrinkage of extracellular fluid volume. It has been suggested that the reduction in serum sodium under such conditions is a compensatory mechanism for a disease-induced reduction in intracellular tonicity, and the provision of extra salt in such cases has no effect on the serum sodium level or on the patient's clinical state.

Although in salt depletion, the chloride level in the extracellular fluid in general falls with that of sodium, the use of the plasma chloride concentration as a criterion of electrolyte deficit is open to fundamental criticism, since the plasma chloride undergoes reciprocal changes with other plasma anions, notably bicarbonate and organic acids, that may occur without significant alteration in the sodium content and hence the volume of extracellular fluid. However, where sodium determinations are not available and it is known that there is no disturbance of acid-base equilibrium, a rough " chloride rule " may be used for calculating the requirements of isotonic saline to restore extracellular fluid volume. Subject to the above reservations, the extracellular

preferably all three plus potassium), ideally every twenty-four hours but certainly after forty-eight hours of treatment. This allows the original estimate of the sodium deficit to be adjusted if necessary, owing to expansion of extracellular fluid volume, etc, and any tendency to abnormality of acid-base balance corrected

Treatment must b

on Prophylaxis

Mixed Sodium and Water Depletion.—Where water depletion as well as sodium depletion is considered to be present as judged from a history of deficient water intake, and from signs such as great thirst, oliguria despite a blood pressure

well as a reduction in extracellular fluid volume, and the introduction of an electrolytically isotonic fluid ... will not allow water to pass from extracellu ... health, the kidneys rarely excrete sodium ... t of normal saline, and the functionally impaired kidneys of salt depletion are even less able to get rid of more salt than water from infused saline so as to provide a surplus of water for restoration of the volume of intracellular fluid.

The correct solution to use in the mixed type of depletion is therefore one that is hypotonic in respect of sodium Half-normal saline (equal parts of isotonic saline and 5 per cent glucose solution) should be infused from the start until an adequate urine flow has been secured, which indicates correction of intracellular dehydration If sodium depletion is still present at this point, as judged from the persistence of signs of subcutaneous dehydration, absence of chloride in the urine and a fall in the serum sodium to a subnormal level, or if there is continuing loss of body fluids, isotonic saline or the appropriate replacement fluid for loss of alimentary secretions can now be given in the amounts considered necessary, plus 2 litres of 5 per cent glucose solution per day to maintain the restored water balance of the patient if water cannot yet be taken by mouth

Disturbances of Acid-Base Equilibrium.—Therapeutic measures directly related to relief of acid-base disturbances, for example the elimination of ketosis in diabetic coma with insulin or the cure of vomiting or diarrhœa, are described elsewhere It is sufficient to mention here only measures whereby restoration of acid-base balance can be assisted until the more direct procedures become effective

Acidosis —In an established acidosis of any degree of severity there will be a relative, and in most cases an absolute, base deficiency It is therefore sound practice to supply extra cations without the corresponding fixed anions in greater amount than that described under the treatment of salt depletion ... as 1/6 molar sodium ... if the patient can ta

but some sort of estimate is desirable at the commencement of treatment. An empirical calculation indicates that in an adult it would require 40 ml of

solution will give 1/6 molar sodium lactate solution. On introduction into the body the lactate ion is oxidized to CO_2 and water, leaving the sodium ion free to combine with bicarbonate ion and so provide extra base.

The rate of administration of the estimated fluid requirements will depend on the degree of peripheral circulatory failure. When this is only slight, intravenous fluids can be given at a steady rate of about 60 drops per minute. But when circulatory failure is so severe as to threaten life, heroic measures are required, and saline should be given at the rate of one litre in the first hour, another litre in the next two hours and a third litre in the next three hours, and thereafter either saline or sodium lactate as indicated, at the rate of one litre every six hours, during which time the daily water requirements can also be met with 5 per cent. glucose solution. It need hardly be added that a close watch must be kept on urine volume and for the development of œdema, especially pulmonary œdema, during this period of repair therapy.

While repair of the existing sodium deficit and provision of the maintenance requirements of water are proceeding, consideration must be given to the problem of making good continuing losses of electrolyte-containing body fluids as they occur It is customary to do so with isotonic saline, except in the case of gastric secretion, where half-normal saline is used, because of its lower sodium content as compared with extracellular fluid. But where the lost body fluids comprise alimentary secretions, disturbance of acid-base equilibrium in the direction of either acidosis or alkalosis is very likely to develop, if not already present. Where kidney function is still inadequate to make the appropriate adjustments to loss of base or acid, isotonic saline will not prevent the onset or aggravation of such acid-base disturbances. To meet this contingency, Cooke and Crowley have devised two solutions with electrolyte contents approximating closely to that of gastric fluid on the one hand and the average of biliary, pancreatic and intestinal secretions on the other.

1. *Gastric Replacement Fluid*

Ammonium chloride 3 745 g. (=70 mEq.)	per litre
Sodium chloride 3 69 g. (63 mEq.)	
Potassium chloride 1 266 g. (=17 mEq.)	

2. *Intestinal Replacement Fluid*

Sodium chloride 5 15 g. (=88 mEq.)	per litre
Sodium lactate 5 60 g. (=50 mEq.)	
Potassium chloride 0·89 g. (=12 mEq.)	

Both fluids are isotonic and can be given intravenously or subcutaneously, and mixed with other fluids such as glucose solution Administration of excess of either ammonium or potassium ion is dangerous, but toxic levels of these ions are entirely avoided if neither solution is given at a rate exceeding 500 ml. (just under 1 pint) per hour The procedure advised is that volume for volume replacements of the appropriate fluid, as judged from the location and reaction of the fluid loss, should be made on a four- or six-hourly basis, the requirement for each period covering the loss of alimentary secretions during the preceding period

Treatment of a case of severe salt depletion is greatly helped if to clinical assessment of the success of repair therapy can be added determination of the serum electrolytes (sodium or chloride plus bicarbonate as a minimum, but

of acid-base equilibrium. Where sodium depletion is present, there is an obvious indication for the infusion of sufficient isotonic saline to repair the depletion and provide the kidneys with sufficient sodium to excrete as the bicarbonate, the [illegible]

this adjustment, tending instead to reabsorb too much sodium. For this reason and because of the postulated shift of hydrogen ions into the cells in place of potassium, repair of alkalosis is greatly assisted by the administration of potassium as well as of sodium ions. Indeed, it has been suggested that potassium is the primary need in alkalosis

Therefore it is advisable in all cases of alkalosis to administer potassium in the amounts and by the methods described below. Paradoxical as it may seem, there is no contra-indication to the oral administration of alkalinizing potassium salts; indeed, this would be the logical therapy if the theory of intracellular acidosis in this condition is accepted

As regards sodium, cases with clinical dehydration and evidence of sodium depletion should obviously be given isotonic saline and glucose solution intravenously according to the estimated requirements as discussed when dealing with the treatment of sodium, or mixed sodium and water, depletion In patients with no clinical or laboratory evidence of dehydration when first seen, [illegible] fluid" of Cooke and Crowley, will be required

Potassium Deficiency.—There are few today who would gainsay that correction of potassium depletion is a valuable and occasionally even a life-saving therapeutic procedure The desirability of giving potassium to patients with a demonstrable need for this ion having been accepted, it remains for consideration as to what quantities of potassium are likely to be required and how these should be given

There are no clinical or routine laboratory guides to the quantitative assessment of the extent of potassium depletion. About 3 g of potassium per day can be lost in alimentary secretions and urine in a patient on continuous gastric suction, it is therefore not surprising that balance experiments have indicated that in severe depletion states a deficit of anything up to 40 g of potassium may accrue. The danger of precipitating a dangerous rise in serum potassium imposes a definite upper limit to the amount of potassium that can be given daily, particularly by parenteral routes. In the writer's experience, up to 6 g of potassium per twenty-four hours can safely be given to patients with major potassium deficits without risk Acceptance of this maximum rate of intake means that it will require some days for restoration of the depleted potassium stores, and one must be guided as to the total amount of potassium to be given by repeated determinations of the serum, and preferably also the erythrocyte-potassium level, daily if necessary, as treatment proceeds. In mild cases, where there is no continuing drain on the body's potassium, a lesser amount, about 3 g daily will be sufficient to repair the deficit in two or three days.

1/6 molar sodium lactate (or its equivalent of 0·56 g. (approx 8 5 gr.) of sodium bicarbonate) to increase the alkali reserve of the extracellular fluid by 1 vol./100 ml. (0 45 milli-equivalents/litre). The number of ml of 1/6 molar sodium lactate theoretically required to restore the depleted alkali reserve to an average normal level of 60 vol /100 ml. (27 milli-equivalents/litre) would therefore be:

$$\frac{40\times(60\text{-determined vol. }CO_2/100\text{ ml.})}{1} \quad \text{or}$$

$$\frac{40\times(27\text{-determined m.Eq. }CO_2/\text{litre})}{0{\cdot}45}$$

This figure is invariably an underestimate, as it does not take into account movement of sodium into the cells or persistence of the factors leading to acidosis; *nevertheless it gives one an approximate figure for guidance.* Since fixed as well as bicarbonate anions are lost with sodium in acidosis, the volume of lactate solution calculated by the procedure described above will not be adequate to make good the all-over sodium depletion. But since it is isotonic, the sodium lactate solution can be included in the total volume of saline considered necessary to repair the all-over sodium depletion; the proportion in which the initial infusion is made should be two volumes of saline to one volume of 1/6 molar sodium lactate solution.

A word of warning is necessary with regard to the treatment of acidosis solely with alkaline sodium salts. In acidosis complicated by a major potassium deficiency, it has recently been shown that owing to disordered function of the potassium-depleted kidneys, such treatment is prone to convert the acidosis into an alkalosis that persists until the potassium deficiency is corrected. The practical point that emerges is that in the treatment of acidosis in which potassium deficiency is suspected or demonstrated from the blood chemistry, the potassium depletion should be corrected along with the acidosis by the methods described below

Alkalosis—*If* conditions in the *extracellular fluid only* were taken into consideration, the apparent need in alkalosis would be for chloride anions to

cellular cation depletion and acidosis, the administration of an acid-forming salt appears in a more unfavourable light. For this reason, and because in

cations Sodium depletion in alkalosis, due to loss in vomitus and in the urine along with bicarbonate in attempted renal adjustment to the alkalosis, varies in degree in different patients. Some show obvious clinical dehydration due to sodium depletion while others do not appear dehydrated and have normal

: measure
vith renal
n content

and hence the volume of extracellular fluid takes precedence over the correction

per litre of water This solution yields approximately 1 4 g. of potassium ions per litre; it can perhaps be used at full-strength subcutaneously, but for intravenous infusion must be diluted with three parts of 5 per cent. glucose [illegible]

potassium given concurrently, a method that in the writer's experience works satisfactorily in practice is to give saline, glucose solution and lactate from one [illegible] cent.) [illegible] which [illegible] iven at [illegible], containing as it does 6 0 g. (154 milli-equivalents) of potassium per litre, must be given very slowly at a rate not exceeding one litre per twenty-four hours. If, as advised earlier, erythrocyte potassium as well as serum potassium levels are determined daily when these relatively large amounts of potassium are being infused, it will usually be found in cases where both levels were reduced that the potassium of the erythrocytes rises to normal before that of the serum. The rate of penetration of radio-active potassium into red cells has been shown to be as low as compared with other tissue cells. It therefore seems a reasonable assumption that by the time the erythrocyte potassium level has been restored to normal, adequate repletion of the general body potassium will have been achieved.

It is therefore advisable at this point to reduce the rate of potassium infusion to about 3 g daily (i e 500 ml of isotonic potassium chloride solution) even although the serum potassium level is still low, and to continue at this reduced rate of infusion until the serum level is in turn restored to normal—in the writer's experience this requires about two more days.

If oral therapy is still impossible and loss of potassium from the body persists, parenteral infusion of potassium must be continued at this lower rate if recurrence of the depletion is to be avoided.

Dehydration in Infants and Young Children.—This subject demands special consideration, not only because of the frequency of diseases leading to dehydration at this age but because of important physiological differences between the water and salt metabolism of infants and that of adults.

1. During the first year of life, the kidneys are relatively inefficient organs of excretion as compared with those of an adult. The urea and mineral clearances are lower per unit of surface area
2. The metabolism of infants is relatively greater than that of adults This leads to the formation of a proportionately greater amount of waste products requiring excretion

These two factors together serve to make the volume of obligatory urine secretion and the insensible perspiration, and therefore the unavoidable water loss, relatively much greater in an infant than in an adult. This explains why infants withstand water deprivation so badly, for their stores of body water are depleted much more rapidly than those of adults

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Although the parenteral administration of solutions of potassium salts has of recent years been elevated to a status of therapeutic respectability, its injudicious use will expose patients to the risk of hyperpotassæmic intoxication with its dangerous cardiotoxic effects. Therefore, where the patient can swallow and retain fluids, oral administration of potassium salts is obviously the route of choice in that the risk of inducing a dangerous increase in the concentration of potassium in extracellular fluid is thereby lessened. But even oral therapy is not without risk in patients where dehydration has led to impaired renal function

tion of these salts to remember that 100 ml. of either a 6 per cent. solution of potassium chloride or an 8 per cent. solution of either potassium acetate, bicarbonate or citrate each yield approximately 3 g of potassium. In mild depletion states, therefore, 100 ml. of any of these solutions should be given daily in divided doses diluted with fruit juice, and double this amount in severe depletion.

But the most severe degrees of potassium depletion are most often encountered in those patients in whom oral therapy is impracticable, owing to prostration, vomiting or because gastric or intestinal aspiration is being carried out. To meet this contingency, methods and solutions have been devised whereby potassium salts can be given subcutaneously or intravenously without danger, provided the following important criteria are observed:

1. A need for potassium must have been demonstrated. Not only is this the only logical reason for giving potassium, but there is experimental evidence that the potassium-depleted subject is more resistant to possible potassium poisoning from over-treatment.

2. *Potassium must never be given intravenously unless the serum level is* known to be low, even in the presence of a known or suspected potassium deficiency.

3. To avoid the risk of a dangerous elevation of the serum level, the initial rate of intravenous administration should never exceed 0·5 g. (about 13 milli-equivalents) per hour, and over a twenty-four hour period half that rate is preferable.

4. It is even more important than with oral therapy that renal function and *urine flow must have been restored to normal before potassium salts are given* parenterally.

The magnitude of the potassium deficiencies met with clinically make it necessary to use parenteral solutions with considerably higher potassium concentrations than in serum if rapid repletion is to be achieved within the limits of the desirable fluid intake. Potassium is given parenterally in the form of the chloride, in one of two ways, either as an addition to the saline fluid being used to correct sodium depletion or as a separate infusion.

Various formulæ for solutions containing sodium and potassium ions have been described, of which the best known is Darrow's "K-lactate" solution —4·0 g. sodium chloride, 2·7 g. potassium chloride and 5·8 g. sodium lactate

TUBERCULOSIS

INTRODUCTION

UNTIL A FEW years ago tuberculosis was one of the most important causes of death in the British Isles and was responsible for more deaths than any other disease between the ages of fifteen and forty-five. Since the introduction of chemotherapy there has been a dramatic fall in mortality in every country from which detailed records are available, the fall being particularly notable in the younger age-groups The outlook for the individual patient has changed immeasurably. Formerly the course of his illness was all too often downwards to eventual death, either by rapid progression or by a tragic staircase of alternate stabilization and relapse. At the present time the newly diagnosed patient, if treated properly, should in the very great majority of cases be able to look forward to the arrest of his disease. He should be able to return to a relatively normal life and his risk of relapse should be small Nevertheless, the effect of the disease on his life may be far from negligible. The young man [illegible] s, some of them in [illegible] ildren. Most will [illegible] For tuberculosis is a social disease, not only in the way it interferes directly with the patient's own life but because of the effect it may have on his family either directly by infection or indirectly through financial or other difficulties

The dramatic advances which have been made in treatment have not been paralleled in the realm of prevention In almost all countries the fall in the notifications of tuberculosis has been only slight It is possible that the notification rate is being kept up by the increased facilities for diagnosis, so that a higher proportion of the actual number of cases of tuberculosis in the community is diagnosed and treated However this may be, no responsible person can be complacent until the notification rate drops as dramatically as the death rate. With the greatly decreased number of deaths and the very slight decrease in cases diagnosed, the number of patients needing treatment and observation has greatly increased For instance, the number registered as needing care has nearly trebled in Scotland since 1942 For a time this put a very great strain on the provision of beds, but, as a result of the decreased length of hospital stay due to better treatment, together with an increased tendency to treat patients at home, waiting lists for hospital beds are disappearing all over Britain At the same time [illegible] Scotland over 50,000.

Because of the decreased risk of infection from milk and the later age of infection from human sources, non-respiratory tuberculosis has decreased impressively over the last thirty years, so that nowadays pulmonary tuberculosis provides the great majority of the cases to be treated. Non-respiratory tuberculosis will therefore receive less space in the following sections

The amounts of water and electrolytes needed to repair dehydration in an infant are even more difficult to estimate than in an adult. The daily maintenance requirements of an infant are about 150 ml of fluid per kg. of bodyweight (2½ fl. oz. per lb.). When dehydration has developed, the infant will have lost anything from 75 to 125 ml. of fluid per kg. Therefore, if the maintenance requirement is added, the amount of fluid needed to repair such deficits must be of the order of 200 to 225 ml. per kg. (3 to 3½ fl. oz. per lb.) per day for at least two days. Such quantities cannot be given by the subcutaneous *route even with hyaluronidase unless some fluid can be given by mouth.* In any case, isotonic saline is the only suitable fluid for subcutaneous infusion—

the technical difficulties imposed by the infant's small veins, the intravenous route with "cut-down" and cannulation of a vein and a slow continuous drip infusion is the only suitable procedure for dealing with a severe dehydration, and should be maintained until oral feeding can be resumed.

The fluid infused must contain electrolytes in amounts sufficient for repair of deficits and later for maintenance, in sufficiently dilute solution to allow for the relatively greater water requirement of the infant. It is advisable to give one-third isotonic saline (i.e. one part of isotonic saline diluted with two parts *of 5 per cent glucose solution) for the first two days and thereafter reduce the* concentration progressively until only one-seventh isotonic saline is being given when the deficit has been repaired and only the maintenance requirements are being met.

the first twelve to twenty-four hours until an adequate urine flow has been established. Thereafter about 20 ml. of isotonic (1.14 per cent.) potassium *chloride per kg per day should be added to the infusion fluid.* The low sodium content of diluted Darrow's "K-lactate" solution is an advantage in infants (for whose treatment it was in fact devised), and a dilution with three parts of 5 per cent. glucose solution forms a very suitable infusion for use during this period

Assessment of progress under treatment is likewise more difficult than in an adult, owing to the difficulty of measuring urine output. Daily weighing of the patient is helpful and much more practicable and informative as to the state of the fluid balance than investigation of the blood chemistry. If urine can be obtained, *estimation of the chloride content of each sample* should be carried out and saline administered until chloride excretion is satisfactory. In this connection it must be remembered that, owing to the lower concentrating power of the infant's kidneys, the desirable chloride content of the urine will be less than in the case of an adult, a figure of 2 to 3 g. per litre being sufficient.

I. A. ANDERSON.

there is no evidence that physical strain is important Many patients on the other hand, seem to develop tuberculosis after a period of mental strain and [illegible] time when purely physical factors were little affected.

Once an individual has overcome a primary tuberculous infection there is good evidence that his resistance against further infection is enhanced. This is the principle underlying the induction of a harmless primary infection by vaccination with BCG (Bacille Calmette-Guérin)

METHODS OF PREVENTION

From what has been said in the preceding paragraphs it will be obvious that in the prevention of tuberculosis there are two main aims. The first is to prevent infection, for without infection with the tubercle bacillus there can be no disease The second is to increase the resistance of the community so that if a person is infected he is more likely to overcome the invader without developing clinical disease.

Prevention of Infection.—In the past there have been two chief sources of infection, cows' milk and sputum.

Infection from Milk.—The tubercle bacilli conveyed by milk are, of course, of the bovine type. These are of similar virulence to human strains. Children are, naturally, most likely to be infected With an alimentary mode of infection the primary lesion is likely to be in the intestinal tract, giving rise to abdominal tuberculosis, or in the tonsil, giving rise to tuberculous cervical adenitis. As [illegible] tion or by obtaining it from herds of cows kept free from tuberculosis, this freedom being ensured by regular tuberculin testing. Britain, and in particular Scotland, formerly had an unenviable reputation for bovine tuberculosis, but great advances have been made in the last twenty years Dairy herds are being freed from tuberculosis area by area, at first by financial inducement to farmers to produce "tuberculin-tested" (T T) milk and then, as the numbers of tuberculin-positive cows decrease, by the slaughter of any found to be tuberculin-positive At the same time the proportion of marketed milk which is pasteurized has steadily increased. By 1954 over 99 per cent of marketed milk in Scotland came either from herds free from tuberculosis or was pasteurized, in England and Wales the figure was about 90 per cent Milk has therefore ceased to be an important source of infection in Great Britain.

Infection from Sputum.—The prevention of infection from sputum is much more complex Although tuberculous infection can theoretically be acquired from patients with discharging sinuses, etc., these sources are so much less important that they will not be considered here Those who are coughing up infectious sputum are vastly more numerous, they are liable to be moving around in the community and, worst of all, many do not know that they have tuberculosis. With the increased facilities now available in Great Britain and the greater efficacy of treatment, it should be possible to isolate all diagnosed cases of infectious tuberculosis and to make almost all of them non-infectious, usually

PREVENTION

INFECTION AND HOST RESISTANCE

Tuberculosis is an infectious disease. At the present time in Britain most people are infected at some time in their lives, as may be shown from the fact that their tuberculin test has become positive. But of those who do become infected only a relatively small proportion develop clinical disease. The outcome of any particular infection will depend on the relation between the host and the parasite Strains of tubercle bacilli differ little in virulence, so that the size of the infecting dose is the most important factor as far as the parasite is con-

Development of disease will also depend on the resistance of the host. The factors affecting host-resistance are numerous. They cannot be discussed in detail here, but some of them must be mentioned because they concern prevention

Though it is difficult to separate genetic resistance from environmental influences, it is probable that races which have been exposed to tuberculosis for

widespread and causes great distress to patients. Age is an important factor. Infants are much more likely to develop disease if infected and are particularly prone to the generalized miliary and meningitic forms. Children from the ages of five to twelve are much less susceptible, but during puberty, adolescence and young adult life resistance is again lowered, progressive pulmonary tuberculosis being the main danger at these ages. After puberty there is a difference in the

milk, butter, margarine and cheese are generally

Overcrowding, as already indicated, increases the liability to massive infection, but the stresses and strains of such an environment probably also lower resistance The same is true of working conditions Occupations involving exposure to silica lower the resistance to tuberculosis. Chronic alcoholism has the same effect, and barmen have a high incidence of tuberculosis.

sedentary occupations. Chronic diseases may lower the resistance to tuberculosis, the most important of these being diabetes mellitus.

The significance of physical and mental strain is much more difficult to assess. Granted sufficient sleep and an adequate food intake for the extra work,

mimicked and it is a wise precaution to have such patients checked. The doctor [illegible]

negative radiographs, but radiography is the only satisfactory way of excluding [illegible]

otherwise unexplained. [illegible]

a [illegible]

c [illegible]

parts of the United States is regarded as the most important method of case finding The third group, which is at present fairly well covered, is that of household contacts of known cases of pulmonary tuberculosis. The primary responsibility for investigating contacts usually lies with the chest clinic in association with the public health services, but the practitioner can do much to [illegible] who should be examined radiologically at regular intervals

For the protection of the public the second group is particularly important, since a patient with unrecognized tuberculosis can disseminate the disease widely. In some parts of Great Britain school teachers, who come into contact with a particularly susceptible population, have voluntarily agreed to be examined radiologically each year Regular radiological examinations are equally important for all other persons dealing with children—nursery nurses, other school employees, etc Other groups which should be included are those who in the course of their work come into contact with a large number of people in the day: food servers; bus and tram conductors, shop assistants; hairdressers; barmen, cinema attendants, ticket collectors, dentists and doctors; all hospital employees The reader can readily extend the list Little has been [illegible]

scale With ordinary methods of propaganda about 25 per cent response is usually obtained, rising to 50 to 60 per cent when intense extra effort is made. [illegible]

within a few months. It is not yet certain how permanent this freedom from infectiousness may be, but present experience is very promising. This conception is relatively recent and is revolutionary from the public health point of view. It makes doubly important the discovery of cases. For if we could dis-

per cent. more cases have been found than were already known to the public health services. Since patients known to be infectious should be adequately isolated and treated, it is from the unknown pool of infection that the main danger arises. The most important preventive measures are those designed to reduce the size of the pool. The aim should be to diagnose all cases of pulmonary tuberculosis at a stage before they become infectious and to ensure by proper treatment that they never become infectious at all.

To put this programme into effect, many difficulties must be overcome. It is

supporting services it is the only quick way to get rid of tuberculosis in Great Britain. Meantime we must deal with the matter within our present context

The principal weapon in a programme of " case finding ", as the discovery of fresh cases is usually called, is miniature radiography in which the films taken

efficiently as possible.

There are two main categories of people whom it is most important to submit to miniature radiography if this preventive weapon is to be used most efficiently. To some extent these two categories overlap. The first category consists of groups which are known to contain a particularly high proportion of active cases. These will give the highest yield of active cases for a given effort. The second category includes groups among whom an unknown infectious case might do most damag

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that three groups yield a proportion of active cases well above the general average. ... due

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... who seems to recover rather

piratory tract infection, who

epsia, or who seems vaguely

ination. Any patient whose

symptoms warrant a barium meal should have a chest radiograph as well; indigestion may be a first symptom of tuberculosis. Neurosis is also easily

engineering which allow adequate ventilation to be combined with adequate warmth are also needed Spread of infection is less likely if a factory population is working in a large number of small rooms than if everyone works in a single large hall. An unknown case will come into contact with many more of his fellow-workers if they all work together in a large hall Although spitting is less frequent than formerly, it is still a sufficiently prevalent habit, especially among elderly men of the lower economic groups, to constitute a public danger which requires to be combated by intensive propaganda

Raising of Host-resistance—Methods of increasing the resistance of the community to tuberculosis will be implicit in the above discussion of the factors underlying resistance. They are mainly matters of social action and of health education. Improved housing conditions will both decrease the chances of infection and also make people more able to withstand it if it occurs The provision of school milk and school meals has done much to improve resistance. But health education is still required to train people, and especially young women, to take diets containing adequate amounts of the "protective foods" already mentioned and to instruct them in the cheapest way of providing these foods. Health education should also stress the importance of adequate sleep and rest, especially for adolescents and young adults, and the value to city dwellers of exercise in the fresh air.

Immunization with BCG.—BCG or *Bacille Calmette-Guérin* is a strain of bovine bacilli attenuated by prolonged growth in the laboratory. The original culture was first isolated in 1908 and continuously sub-cultured until it was first used in man in 1922 The aim of vaccination is to increase the patient's resistance by an artificial primary tuberculous infection due to an organism which causes only a local lesion with some swelling of the draining glands Therefore *BCG is only suitable for those who have never been infected and are tuberculin* negative. It is calculated that more than sixty million people throughout the world have been vaccinated, mainly since 1945, but the vaccine has only comparatively recently been introduced to the British Isles. The initial policy was to vaccinate those especially exposed to infection, such as contacts of known cases of tuberculosis, nurses and medical students More recently this has been extended in many areas to children who are about to leave school. There is a great deal of evidence suggesting the value of BCG vaccination, though few carefully controlled trials have been carried out But a recent large-scale controlled trial among urban school-leavers in England has conclusively shown the value of

[illegible] carried out by injecting

[illegible] In the Danish vaccine

[illegible] After two to three weeks

[illegible] cination. It gradually

[illegible]

of BCG is a glandular cold abscess which occurs in a very small proportion of cases. This was commoner when infants were vaccinated on the leg; with vaccination on the arm the incidence of glandular abscess is very low. When an abscess occurs it is readily treated by aspiration and instillation of strepto-

the public to co-operate, but it must be realized that experience has shown that the incidence of tuberculosis is higher in those who fail to volunteer.

So far in this country miniature radiography has been mainly used for surveys of workers in factories, offices, etc. Often the surveys are carried out once a year, but experience has shown that such frequent visits give a relatively low return unless there is a rapid turn-over of workers. It is recommended that such examinations should take place every three years.

Case Finding by Tuberculin Testing.—In certain areas where there is a low prevalence of tuberculosis, such as in Minnesota, U.S.A., and in certain parts of Norway, it has been found useful to carry out regular tuberculin tests on the population and to subject the positive reactors to radiological examination at frequent intervals. This is only a practicable procedure with excellent public co-operation and a low incidence of positives. At the present time it is not worth doing in this country. An alternative method has been to carry out tuberculin tests on children when they first attend primary schools at the age

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ol, both

may be decreased by the proper management of known cases of tuberculosis and by ensuring that the members of the community live, work and play under conditions

With modern methods of treatment, properly applied, it should be possible to convert the sputum to negative in almost every case within six months. In hospital, special precautions are taken about the disposal of sputum and it is usual for nurses to wear masks and gowns, at least when handling patients and making beds. It is very unusual for nurses in a tuberculosis hospital to develop the disease, probably because their health is carefully watched and most hospitals ensure that they have a positive tuberculin test, either as a result of a previous healed primary infection or as a result of BCG vaccination.

Formerly there was a shortage of beds for tuberculosis and many patients had

in the closest co-operation with the family doctor, who retains, of course, primary responsibility for all aspects of the patient's welfare and for that of his family

The chances of an unknown open case of tuberculosis infecting others are closely related to the factors of space and ventilation. It must be remembered that in winter no one is going to endure draughty ventilation without adequate heating. Adequate public health standards are required in houses, places of work, and in cinemas, theatres and other places of entertainment. Standards of

to destroy the patient's population of tubercle bacilli or to reduce it to numbers which it is certain that the patient's own resistance can handle.

Bed-rest and the Sanatorium Régime.—As indicated, some physicians are now doubting the necessity for bed-rest if satisfactory chemotherapy is available There is so far no incontrovertible evidence on the subject and most

careful grading of exercise need be less meticulous and the patient is allowed much more latitude after he leaves hospital Fresh air, no longer one of the mainstays of treatment, is nevertheless regarded as a valuable tonic for those with a long-term illness and a useful precaution against infection of attendants There is, however, no reason to " freeze the tubercle bacillus out " in the winter; adequate warmth should be provided

Diet.—
appetites
quantities
margarine. Vitamin supplements are unnecessary

the day.

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family is to leave the job half done Rehabilitation, the fitting of the patient for return to ordinary life, should be first considered soon after diagnosis Nowadays it is much easier than formerly, for most patients can return to their former employment and the chronic patient with a positive sputum should no longer be a problem But some patients may need training for some other job, and it may be possible to start this in hospital The advice of an almoner or social worker should be fully utilized in connection with this and all other social aspects of the

Org[illegible] **of Treatment**

fully to him when he is first diagnosed In addition, the knowledge that the patient will remain under his care and can be readmitted if necessary often enables the physician to curtail the period in hospital. The patient himself

mycin (see p. 69). Lupoid reactions to vaccination have been described, but are very rare indeed Among the *many million people vaccinated with BCG only* one or two deaths with disseminated disease, probably due to the bacillus, have been recorded. The risk of the vaccine therefore is infinitesimal in comparison to the risk that it is designed to avert.

Before vaccinating contacts of known tuberculous cases a tuberculin test is [illegible]

weeks' period is still negative, then the patient is vaccinated. In order to avoid infection during the six weeks' waiting period, the individual should not come into contact with the tuberculous patient during that time. After vaccination the tuberculin test will usually become positive in about six weeks. Until this *has occurred, the individual is not effectively protected and he should still be* kept away from any known case of tuberculosis. Normally the original case will have been removed to hospital so that no difficulty will arise. In the case of an infant of a tuberculous mother the problem is slightly different. The infant should be removed from the mother at birth, before there is any chance of his becoming infected, and he can be vaccinated shortly afterwards. He must remain separated from the mother until the tuberculin test is positive. These *rules must be interpreted with common sense. Where tubercle bacilli have* never been recovered from the patient and he is being treated at home it is an unnecessary disruption of the family to demand that the contacts should be separated for three months.

Vaccination with the Vole Bacillus.—The vole bacillus is a form of tubercle bacillus confined to voles. It is not pathogenic to man, but when injected intradermally results in a lesion similar to that of BCG. Experience with the vole *bacillus is very much less than with BCG and the vaccine is not yet released for* general use.

THE TREATMENT OF TUBERCULOSIS

GENERAL PRINCIPLES

In the last few years the treatment of tuberculosis has undergone a revolution which is still proceeding. Chemotherapy has evolved from a mere adjunct to other forms of treatment towards becoming the dominant factor. Surgery has been increasingly employed in pulmonary tuberculosis, though there are signs that, with the success of long-term chemotherapy, it may be less used in future. As a result of these advances certain long-established treatments, such as artificial pneumothorax, have fallen into disrepute. Even the value of bed-rest *and the sanatorium régime* is being doubted. The reason for this is clear. We [illegible]

the bacillus directly and can keep up this [illegible] the very great enhancement of therapeutic potential the patient's resistance has become relatively less important to actual treatment, though it may well remain of importance in preventing relapse. The aim of treatment must now be either

lined some of the characteristics of the individual drugs. Drug combinations will then be discussed.

[illegible]

intramuscular injection, sometimes 1 g is given two or three times a week. For children the daily dose is 30 mg. per kg of body-weight Intrathecally, in [illegible] cts are dis- [illegible] Deafness [illegible] mage from streptomycin gives rise to giddiness. The incidence is very low under the age of forty, but appreciable in older people. By giving intermittent dosage, as indicated later, this can be largely avoided A modification, dihydrostreptomycin, has been advocated as causing less vestibular damage, but is much more [illegible] mycin at all.

Hypersensitive reactions are not uncommon with streptomycin. They usually occur within four weeks of starting treatment, but occasionally later. [illegible]

rash have subsided Antihistamine drugs may be of some value in a severe reaction A test dose of streptomycin should then be administered; if the [illegible]

desensit [illegible] given [illegible] smaller [illegible] be a mild reaction and the previous day's dose will have to be repeated or the patient even given a day's rest. It is usually possible to desensitize a patient within two to three weeks. Very rarely the reactions are so severe that desensitization has to be carried out under cover of cortisone or corticotrophin (see p. 79)

[illegible] sensitive organisms. Resistance can be avoided in almost all cases by giving PAS or isoniazid in appropriate doses at the same time (see below)

Isoniazid (isonicotinic acid hydrazide) —This is a synthetic drug. It is given by the [illegible] standard do[illegible] the daily do[illegible] meningitis u[illegible]

feels confident that the physician is familiar with all aspects of his case. It is also easier for the chest physician to co-operate closely with the general practitioner.

For geographical reasons this arrangement is not always possible. In that case it is most important that there should be the closest consultation between hospital and clinic [illegible] doctor should be fully [illegible] ued after the patient [illegible] igh the general practitioner, who should ensure that the patient carries out his treatment meticulously. This is particularly important, as an error may result in the emergence of tubercle bacilli resistant to the drugs and the patient's whole future may be compromised.

As hospital beds should now be readily available, in general a patient with a positive sputum should not be treated at home until he ceases to be infectious. When home treatment is undertaken, there must be the closest co-operation between chest physician and family doctor, and the Health Visitor must make frequent visits to ensure that treatment is being properly carried out and that suitable precautions are being taken against infection of other members of the household. It is desirable for the sake of morale, and to check that the drugs are having no toxic effects, for the chest physician to visit the patient at home two weeks or so after starting chemotherapy and thereafter as necessary, though the patient will have to be brought by ambulance to the clinic for chest radiography, etc., at regular intervals.

Treatment abroad, though formerly so fashionable, is now much less popular. Medical standards are at least as good in this country and the pleasures of being in a mountain sanatorium may not compensate for the distance from family and friends.

CHEMOTHERAPY

Formerly, when single drugs were used the tubercle bacilli of many patients became resistant to the action of the drug within a few weeks or months. Nowadays it is known that, by using proper combinations of two or more drugs, drug resistance can be avoided in almost all cases. There are only a few combinations which are highly effective in preventing the emergence of resistant bacilli. Dosage is also important, especially in the case of PAS (para-aminosalicylic acid). Errors on the part of either the patient or the doctor may therefore have very serious consequences, as the organisms, once resistant, are usually permanently so. The patient's whole future treatment may be jeopardized. [illegible] and remai[illegible] case until [illegible] acilli is so reduced that he is sure the patient will be able to handle the residue with his own defences This is not always easy to estimate It is wise therefore to be on the safe side and give too much rather than too little.

[illegible] generally acce[illegible] etimes kno[illegible] drugs are used only when, owing to previous unsatisfactory chemotherapy or to primary infection with a resistant organism, the patient's bacilli are resistant to one or more of the standard drugs In the following paragraphs will be out-

blood potassium have occasionally been recorded in patients taking PAS. Some of these have probably been due to liquorice used as a flavouring agent, for liquorice has an effect like deoxycortone acetate.

In the past the clinical importance of PAS drug resistance has not always been appreciated. Laboratory tests for PAS resistance are technically difficult and the clinician may be confused by varying reports on successive cultures from the same patient In practice it is more likely that a strain which behaves clinically as if it were PAS resistant will be reported as the result of *in vitro* testing as " sensitive " than that the reverse will occur. In any patient whose past experience of chemotherapy gives reason to doubt the PAS sensitivity of his tubercle bacilli, it is wise to test at least three or four different cultures before pronouncing the strain sensitive. If any of these cultures shows as resistant on the *in vitro* test, the patient's bacilli should be regarded as PAS resistant even if other cultures are reported as " sensitive ". It is wise, of course, to confirm an unexpected finding by further tests.

It has been established that PAS resistant bacilli commonly emerge if the [illegible]

should be sought The other drugs at present available are in general less effective, more toxic and more expensive. Their correct use requires judgment and experience Some of them are mentioned briefly below

Viomycin.—Viomycin is an antibiotic with very weak anti-tuberculous properties It has important toxic side-effects. It should be given only to those whose bacilli are resistant to standard drugs.

Oxytetracycline (Terramycin) —This drug has a very weak anti-tuberculous effect. In doses of not less than 2 to 2 5 g twice a day by the mouth it has been shown to delay the emergence of resistance to streptomycin and isoniazid. In this respect it is less effective than the three standard drugs.

Pyrazinamide and Cycloserine (oxamycin) —At the time of writing these are not available for general use Both are toxic and seem likely to have no advantages over the present standard drugs They may prove to have a place in the treatment of the few patients whose organisms are resistant to all three standard agents

Cortisone and Corticotrophin.—The place of cortisone and adrenocorticotrophic hormone in the treatment of pulmonary tuberculosis is as yet un- [illegible]

effective anti-tuberculous chemotherapy. Cortisone has been found of value in patients with tuberculosis who are admitted desperately ill and seem likely to die within a few days. Such patients may die before anti-tuberculous chemo-

the drug sometimes gives rise to peripheral neuritis, as shown by burning feelings and paræsthesiæ, but in the usual doses isoniazid has almost no toxicity. Even hypersensitivity reactions are very rare.

If isoniazid is given alone, tubercle bacilli become resistant to it even more readily than to streptomycin. But this can be avoided by giving it with streptomycin or with PAS. If the patient's bacilli are already resistant to these drugs, oxytetracycline may be used, but is less effective and very expensive.

PAS (para-aminosalicylic acid).—PAS is a synthetic drug. It is well absorbed from the intestinal tract and is therefore given orally. It is less effective against tubercle bacilli than either streptomycin or isoniazid and its main use is to prevent the emergence of resistance to these drugs. It is usually

to attain the maximum effect in the prevention of streptomycin resistance. Administered with isoniazid, a dose of 5 g. twice a day is effective. For children the daily dose is 0·5 g. per kg. of body-weight if administered with streptomycin, though 0·35 g. per kg. is sufficient to prevent isoniazid resistance.

The chief toxic effect of PAS is nausea. When severe, this may lead to vomiting. Loose stools are also common. The drug is available in various special preparations designed to avoid these effects, but not all such preparations are fully absorbed. The most reliable ways to give PAS are either in tap water or in rice-paper cachets, containing 1 to 1·5 g., which are dipped in water and swallowed with the aid of a draught of fluid. When 20 g. of sodium PAS is to be given each day it is wise to begin with a daily dose of 10 g. and increase slowly, attaining the full dose in five or six days. If nausea occurs, the dose may be lowered for a day or two and then again slowly increased. It often helps to take the drug towards the end of a meal. If loose stools are a serious trouble small doses of tincture of opium may be given for a short time and then gradually reduced. With the smaller dose of 10 g. a day, much less trouble occurs.

Hypersensitive reactions are quite common with PAS. The usual manifestations are similar to those of streptomycin sensitivity and they occur about the same time after starting treatment. If it is not realized that the fever is due to hypersensitivity and the drug is continued, liver damage with severe jaundice may occur and the rash may go on to exfoliative dermatitis. In severe cases symptoms of encephalitis may ensue. The patient may not uncommonly

Tests must therefore be

The normal test dose for

re one it may be wise to

by the mouth and the

reactions to be expected are the same as those with streptomycin. In a mild case it is sufficient to start desensitization with a dose of 0·5 g., but in severe cases this will have to be reduced to 0·1 g. or less. In some patients reactions even to low doses are so frequent that desensitization has to be covered with cortisone or corticotrophin (see p. 79). But usually it is quite feasible to start with 0·5 g. a day and increase by daily increments—1, 1·5, 2, 2·5, 3, 4, 5 g., etc.—completing the process within two to three weeks.

PAS has an antithyroid effect. When given in high dosage for more than six

four times daily, keeping isoniazid in reserve As the combinations already mentioned are so effective in preventing drug resistance, it now seems less

the emergence of drug resistance in perhaps 10 to 15 per cent. of cases They are not therefore recommended, and when any patient has a history of having received such treatment it must be remembered that his organisms may be resistant to either or both of the drugs used *A careful history of previous chemotherapy should always be taken* If any drug has been given alone, or indeed if there has been any deviation from the combinations recommended, specialist advice should be sought.

PRIMARY TUBERCULOSIS

In patients with primary tuberculosis presenting for treatment the primary complex is usually in the lung and hilar lymph glands This is partly because primary lesions in the lung are much more common, especially nowadays with the increased safety of milk, partly because primary lesions elsewhere are less easy to diagnose. If the primary lesion has been in the tonsil, for instance, the tonsillar lesion is not usually obvious and the patient presents with cervical lymphadenitis (see p 139). If the lesion is intestinal it will be diagnosed, if it is diagnosed at all, as abdominal tuberculosis (see p. 139) Rarely a primary lesion may present as an ulcer of the skin or mucous membrane with enlargement of the regional glands The diagnosis usually has to be made by biopsy. Such a lesion responds excellently to chemotherapy, which should be given as outlined below.

Primary Pulmonary Tuberculosis.—In primary pulmonary tuberculosis in children the glandular component of the primary complex often predominates. The lymph glands may erode through the wall of a bronchus resulting in so-called "epituberculosis". Epituberculosis is a convenient word which refers

collapse of a lobe or segment, an exudative lesion of segmental or lobar distribution, or a caseous pneumonia Any combination of these three may occur and it is not easy to tell from the radiological appearances which predominates in any particular case The lesion of epituberculosis may not necessarily be in the same anatomical part of the lung as the pulmonary component of the primary complex

Primary pulmonary tuberculosis can only be diagnosed from later post-

usually in such cases it is therefore not possible to differentiate between primary and post-primary pulmonary tuberculosis These patients should be treated in the same way as adults with post-primary pulmonary tuberculosis (see p 133)

therapy is able to become effective. With cortisone treatment patients may improve much more rapidly than would otherwise be the case. A dose of 25 mg. *may be given four times daily and continued for six weeks or more.* Corticotrophin should be given once a fortnight and the precautions of cortisone therapy observed (see p. 79). Anti-tuberculous chemotherapy must always be given at the same time.

Calciferol.—Calciferol is of established value in the treatment of lupus vulgaris. It has also been given in the treatment of tuberculous lymphadenitis, but here its value is uncertain. If the dose does not exceed 1,100 units per kg. daily, there are usually no toxic effects, but it is wise to check the serum calcium at intervals.

Drug Combinations.—Anti-tuberculous drugs are always given in com*bination in order to prevent the emergence of drug-resistant tubercle bacilli.* Unless the patient has been infected with drug-resistant organisms from another patient, the drug combinations to be mentioned are effective in almost all cases in preventing the emergence of resistance however long the drugs are continued. But if the patient has received chemotherapy previously in doses and combinations other than those mentioned here, his organisms may have become drug resistant and specialist advice should be sought as to the best treatment. Before treatment is begun at least two specimens of sputum should be sent for culture in order that drug-resistance tests may be done. If the past chemotherapy [illegible] five or six specimens should be sent.

[illegible] *is not usually*

[illegible] se to repeat the resistance tests once a month as long as the sputum is positive. Whether or not monthly tests are feasible, the last positive culture should certainly be kept for a month or two so that it can be tested.

[illegible]

except tuberculous meningitis, which will be dealt with separately. [illegible] where infection with drug-resistant organisms is not uncommon, owing to the *previous extensive use of unsatisfactory chemotherapy,* it may be wise to add sodium PAS 5 g by the mouth twice daily. All three drugs are given until the [illegible] tests become available. If the organisms prove to be sensitive

[illegible] forty run some risk of

[illegible] The risk of vestibular damage can be very greatly reduced by giving 1 g. streptomycin three times weekly instead of daily, but if this is done, both PAS and isoniazid, in the doses already *mentioned, should be given daily. Otherwise isoniazid-resistant* [illegible]

[illegible] ed at home,

[illegible] PAS and isoniazid may be administered in the doses already mentioned. It is convenient to give both drugs together in rice-paper cachets. In this way the patient is unable to take one drug without the other. Nevertheless, it must be impressed on him that *it is important to take the full dose.* Isoniazid-resistant organisms have emerged in patients who have taken less than the full dose even though the PAS was reduced proportionately to the isoniazid. Some physicians prefer to use a combination of streptomycin 1 g. daily together with 5 g sodium PAS given

tuberculosis is excellent even though the radiological appearances may persist for a year or more. The only definite indication for resection is clear evidence of a persistent destructive caseous broncho-pneumonia confined to a limited area of the lung Some authorities have recommended the resection of epituberculous lesions persisting for a year or more, and have even, as a prophylactic measure, dissected out enlarged hilar glands in the early stages of the disease. This practice is not recommended

Erythema Nodosum.—Erythema nodosum is often associated with primary tuberculosis, but may also be associated with other conditions. The patient over the age of puberty with erythema nodosum and primary pulmonary tuberculosis is more likely to develop progressive post-primary pulmonary tuberculosis than is the patient with primary disease and no erythema nodosum. Chemotherapy should therefore be given to such cases Below the age of puberty there is less evidence that erythema nodosum carries any higher risk of later tuberculous complications. Nevertheless, it is probably wiser to give chemotherapy If the patient with erythema nodosum, whatever his age, has a positive tuberculin test and a normal chest radiograph, it is reasonable to withhold chemotherapy, but he should have a radiograph of the chest at intervals of not more than three months for at least two years

In the acute stages the patient will require to be kept in bed Whether bed-rest is necessary thereafter depends on the lung lesion and not on the erythema nodosum. Sometimes a patient with erythema nodosum may continue to run a high temperature with recurrent crops of skin lesions, perhaps with swollen joints This is especially common in middle-aged women. In such cases, if the erythema nodosum is associated with tuberculosis, the response of the temperature and other symptoms to chemotherapy is usually dramatic. When undertaken it is wise to continue the chemotherapy for at least a year.

MILIARY TUBERCULOSIS

Once a diagnosis of miliary tuberculosis has been made the treatment is [illegible]

diagnosis is made, a lumbar puncture should be done. If the cerebrospinal fluid is normal, the lumbar puncture should be repeated weekly for the first [illegible]

usually kept in bed for six months or so. There seems much less reason for prolonged rest in bed now and he can be allowed to get out of bed for increasing periods as soon as his general condition permits. As any hiatus or error in [illegible]

The following paragraphs therefore refer to the treatment of primary pulmonary tuberculosis in children.

Rest in Bed.—Children with primary tuberculosis are best treated at home, provided that the social conditions are satisfactory and that this does not involve leaving the child in continued close contact with an infectious case. It is undesirable to separate a child from his home surroundings for long periods if it is avoidable. Rest in bed is probably much less important in primary tuberculosis in childhood than in tuberculosis in the adult, but if the child is ill or if there are extensive changes in the radiograph he should be kept at rest in [illegible]

lesions of epituberculosis may actually develop while the patient is receiving chemotherapy. Such extensions are probably due to mechanical factors, caseous material being discharged from a gland into the bronchial lumen, resulting in an initial collapse in the area of lung concerned. This may be followed by an exudative lesion due to hypersensitivity to tuberculo-protein contained in the caseous material. But caseous pneumonia, which may result in permanent changes, is unlikely to occur while the child is on chemotherapy. On the other hand, if the lung component of the primary complex is large or progressive, it appears to be affected by chemotherapy in the same way as a post-primary lung lesion.

[illegible] should definitely be given if the child is ill, [illegible] 's of [illegible] uch [illegible] ary [illegible] e of [illegible] per- [illegible] are [illegible] that there is an increased risk of disseminated tuberculosis; [illegible] is to prevent later post-primary complications. The incidence is small apart from [illegible] that chemotherapy is there- [illegible] re given in the doses and [illegible] le harm is likely to ensue, [illegible]

Bronchoscopy.—In the presence of epituberculosis, bronchoscopy has been used to suck out the caseous material discharging from the gland into the bronchus. It usually has only a very temporary effect; the gland continues to discharge and the bronchus soon becomes blocked again. The only definite indication for bronchoscopy is secondary infection occurring beyond the block.

Surgery.—Most physicians consider that the prognosis for primary pulmonary

10 mg per kg per day This is a much higher dose than that normally given; it is known to be highly effective, but it is not yet known whether a lower dose would suffice. Complications of the high dose are very unusual in children. Rarely peripheral neuritis may occur in adults This takes the form of pain and burning sensations in the limbs It is claimed that pyridoxine, 50 mg. three times daily, given from the start of treatment, will greatly reduce the incidence PAS and isoniazid should be continued for at least a year, though the dose of isoniazid can be lowered to 3 mg. per kg. after the first six months In mild early cases the [illegible]

[illegible]

most important criterion is cerebrospinal fluid sugar. It is desirable that this should rise to a level consistently above 50 mg. per 100 ml before the patient leaves hospital It may be anything [illegible]

is a[illegible]

The[illegible]

20 per cu mm As soon as the patient is relatively well clinically, he may be allowed out of bed for increasing periods. If his home is good and the sugar in the cerebrospinal fluid has returned to normal, it may be possible to discharge him after about six months' hospital treatment, although he will have to return for lumbar punctures every one to two weeks The physician must, of course, be confident that the treatment will be [illegible]

In the few patients who deter[illegible]

[illegible] It should be carried out only in special centres It is probably life-saving in a few cases.

The majority of patients who recover from tuberculous meningitis do so completely Occasionally there is residual mental impairment or some other residual neurological lesion After a year's treatment, or sometimes a little longer, the adult is usually fit for work or the child for school Where teaching is available in the children's ward, the patient can start lessons as soon as he loses his clinical symptoms.

PULMONARY TUBERCULOSIS

Patients with a positive sputum should be treated in hospital at least until the sputum becomes negative. It may be justifiable to treat at home a patient whose sputum is negative, providing the social conditions are satisfactory and he seems likely to obey instructions Normally the patient is treated by rest in bed in the first place, being allowed up for toilet purposes unless he is really ill In most cases at least three months' bed-rest is advisable, but with extensive disease the period may be very much longer, especially when cavities remain unclosed As soon as the preliminary investigations have been completed, the patient will be started on anti-tuberculous chemotherapy in one of the doses and combinations already outlined. The optimum duration of chemotherapy is still uncertain, but the results have been greatly improved and the relapse rate greatly reduced by prolonged treatment. Chemotherapy will normally be carried on after the patient leaves hospital and even after his return to work The minimum duration in the case of pulmonary tuberculosis should be a year, and

The results of treatment for miliary tuberculosis are now very satisfactory, though a few patients, if they are admitted desperately ill, die in the first few days or weeks. The use of cortisone, in addition to chemotherapy, may save some of these (see p. 79). Infants are often diagnosed late and have a higher mortality than older children. Since the introduction of isoniazid, later complication by meningitis is most unusual. Most cases who survive the first few weeks are likely to make a complete recovery. But it must be remembered that the miliary disease is disseminated throughout the body and it is most important to ensure that the tubercle bacilli are effectively suppressed everywhere. It is for this reason that at least a year's chemotherapy should be given, and if there is any doubt about the rapidity of clearance of the lesions the treatment should be continued for longer.

TUBERCULOUS MENINGITIS

The treatment of tuberculous meningitis has been revolutionized by the introduction of chemotherapy. Formerly virtually all patients died. At present, with proper treatment, 75 to 80 per cent. or more recover. The chances of recovery depend largely on early diagnosis. If treatment is started while the patient is conscious, the prognosis is good, but if the diagnosis is only made when the patient is unconscious, the prognosis is very much worse.

The treatment involves skilled nursing, and there is no doubt that it is better carried out in special centres where experienced medical care is available. A patient who is unconscious or suffering from severe cerebral irritability may be a difficult nursing problem. He is probably very wasted and both his skin and his mouth will require constant attention. Feeding is frequently a problem. With patience and persistence it is usually possible to feed with a spoon, but occasionally tube feeding may be necessary.

Chemotherapy should be started immediately on diagnosis. Intramuscular streptomycin reaches the cerebrospinal fluid only in relatively small concentrations. In consequence it was found that better results were obtained if the drug is given intrathecally. This of course involves frequent, even daily, lumbar punctures over a long period. With the introduction of isoniazid, a highly effective drug which reaches the cerebrospinal fluid in relatively high concentrations when given by the mouth, the question was raised whether intrathecal streptomycin was still necessary. It has not yet been established that the results are as good when no intrathecal streptomycin is given. But it has been shown in a controlled trial that when intrathecal and intramuscular streptomycin is given for no more than the first week, together with isoniazid and PAS by the mouth for a very much longer period, the results are as good as

dose of streptomycin should be 0·1 g. for adults or for children over ten y old, 50 mg. for those between one and ten and 25 mg. for children under the age of one year. The drug should be dissolved in 2 to 3 ml. of sterile normal saline and injected slowly, being mixed with cerebrospinal fluid as it is injected. The intrathecal injections are given daily for the first week only. Intramuscular streptomycin in the usual doses is also given for the first week. From the beginning of treatment oral PAS, in the usual dose, is combined with isoniazid

case The nerve is exposed by dissection as it crosses the lower third of the anterior scalene muscle and then crushed. The paralysis usually lasts for about six months, but in perhaps 20 per cent. of cases it is permanent. In view of the considerable diminution of lung function which results, many physicians have

operation continue to be excellent, but many patients who formerly would have been treated with thoracoplasty are now having their lesions resected with as good results Briefly, the operation is designed to relax the upper part of the lung This is achieved by subperiosteal resection of portions of the upper ribs and by dissecting free the apex of the lung, carrying this as far down as the hilum on the medial side The residual periosteal portions of the ribs are allowed to fall downwards and inwards. When the bone re-forms, the volume of the apical part of the
retained in a p
periosteal porti
six weeks in or
bone has formed
according to the ar
ribs which have to
in the first stage If more than this number have to be resected, a second or third stage is necessary. Some surgeons have abandoned all but the limited single-stage operation Others in order to reduce deformity, are leaving the first rib intact

necessary to remove both the upper lobe and the apex of the lower lobe there may be some difficulty in closing the subsequent space. Some surgeons therefore carry out a preliminary thoracoplasty so as to reduce the volume of the thorax before the resection is performed Thoracoplasty may also sometimes be necessary subsequent to resection when it has proved impossible to obliterate the residual space with the remaining lung tissue. It may also be used to help to close an empyema space

Usually the patient will have been prepared
by at least three months'
operation until the patien
bacilli are resistant to the standard drugs it may be necessary to carry on without these criteria being fulfilled.

in severe cases it should be continued for two years or even more. It is wise to persist for at least a year after the last positive sputum culture or after the last cavity has closed, whichever is the later. There are a few patients whose cavities prove impossible to close by the normal methods and who are unfit for surgery, owing to extensive disease, advanced age or poor lung function It has been found that such patients can be kept sputum-negative, at least for long periods, by anti-tuberculous chemotherapy. The minimum period of treatment required to prevent relapse has not yet been determined, but it probably exceeds two years. Chemotherapy is most effective in acute exudative disease, but has a slower effect in other types. With prolonged chemotherapy probably 60 per cent. or more of cavities close as the result of rest in bed and chemotherapy only. If cavities are going to close, they will usually do so within six months. In chronic fibrotic disease the radiological response to treatment is very much less impressive. Nevertheless, in almost all cases it is possible to make the sputum negative and it should be possible to keep it negative either by supplementary surgery or by prolonged chemotherapy.

The patient should stay in hospital until his sputum is persistently negative on culture and preferably until all cavities have closed, unless the latter is thought unlikely. In deciding on discharge, the social conditions of the patient and his capacity for self-discipline must be taken into account.

The prognosis in pulmonary tuberculosis is dominated by cavitation. Before the introduction of chemotherapy a patient with a residual cavity was almost certain to relapse. Since the use of chemotherapy relapse is less certain, but nevertheless every effort must be made to close or remove cavities. This is the chief aim of collapse therapy and resection.

[illegible] ed, in [illegible] ioned. It consists of the introduction of air between the two layers of the pleura, allowing the lung to contract and often resulting in the closure of a cavity. The air space has to be maintained by regular refills, usually given once a week or once a fortnight. Artificial pneumothorax was commonly maintained for three years or more. It has been largely abandoned partly because equally good results are obtained by prolonged chemotherapy; partly because of the accompanying risks of air embolus, hæmothorax and tuberculous empyema; and partly because of the inconvenience to the patient

Artificial Pneumoperitoneum.—The place of artificial pneumoperitoneum in the treatment of pulmonary tuberculosis is at present uncertain. In some centres it is regarded as of great value, in others its use has been abandoned. It is most commonly used for extensive bilateral lung disease, for cavities at the base of the lung or for those in the apex of the lower lobe. It has fewer complications than artificial pneumothorax, air embolism is less common and peritoneal effusions are comparatively rare.

If air is introduced into the abdomen it tends to collect under the diaphragm. As air refills are given the intra-abdominal pressure rises and both leaves of the diaphragm also rise, resulting in relaxation of both lungs. Pneumoperitoneum is not usually maintained for such long periods as pneumothorax. Often it is kept going for one or two years only. Weekly or fortnightly refills have to be given. For technical details of induction and refills a specialized textbook should be consulted.

Phrenic Nerve Paralysis.—In some centres unilateral phrenic nerve paralysis

patient in bed for one to three months and then to rehabilitate him gradually. *The duration of post-operative chemotherapy will depend partly on how long* chemotherapy has been given before operation and partly on the amount of residual disease Three months' chemotherapy after operation should be a minimum, and in many cases six months or more may be indicated Most [illegible] operation and can [illegible] bouring.

[illegible] ionary tuberculosis is very much less difficult than formerly. The patient is often off work for less than a year and his previous employment is often available to him. Although it is probably undesirable for patients with severe disease to return to posts involving heavy physical work, it is now unnecessary to subject patients to the years of semi-vegetable existence which used to be their lot. If the work to which the patient must return is likely to involve strain, this should be an indication for prolonging the period of anti-tuberculous chemotherapy after his return to work rather than damaging the patient's life and career by inducing *him to give up work for which he may have received special training and in* which he may have had long experience Nowadays ex-tuberculous patients do not seem to be more frequently absent from work than other people and make excellent employees However, some individuals do present rehabilitation problems. Such patients have usually been ill for a number of years, or have been regarded as incurable or have only recently received the benefits of the advances in treatment now available With these there is the problem of readjustment to the prospect of once more leading a normal life which the patient after his long years of invalidism may regard with some apprehension. There is also the problem of training the patient for useful work This matter should be considered as soon as a therapeutic programme is outlined. It may be possible to arrange some preliminary training while he is in [illegible] little purpose in special settlements for tuberculous patients, which were desirable enough when many patients remained sputum-positive for the rest of their lives but which are less necessary with the more successful modern treatment Sheltered workshops should also hardly be necessary except for *patients who suffer from bronchitis in addition to tuberculosis.*

Further Observation.—Relapse in pulmonary tuberculosis can be detected early only by radiography of the chest or by sputum examination Even though the relapse rate is now very greatly reduced, it is important for the patient to *have regular follow-up examinations for a prolonged period If* he is still on chemotherapy he should be seen every six to twelve weeks, thereafter at first every three to four months, later every six months, until the disease has been quiescent for at least five years Even after that it is wise to see him at least once a year for the rest of his life. He should have a chest radiograph at each attendance and if sputum is present a specimen should be sent for examination and culture

TUBERCULOUS PLEURAL EFFUSION

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Lung Resection.—Since the introduction of anti-tuberculous chemotherapy, lung resection for tuberculosis has become relatively safe. Segments, lobes or even the whole lung may be removed. It is desirable if possible to prepare the patient by a course of chemotherapy of three months or more and it is best that the patient's sputum should be negative at the time of operation Once again, if the patient's organisms are drug-resistant it may not be possible to fulfil these criteria. In such a patient the operation carries a higher risk of subsequent complications. If possible it should be covered with a combination of anti-tuberculous drugs to which the patient's organisms are sensitive, even though these be less effective than the standard drugs. When the resection has to be extensive, it may be necessary to reduce the volume of the thoracic cage either by a preliminary thoracoplasty or by temporary phrenic crush at the time of operation.

The main indication for resection is a residual cavity or cavities which it has been impossible to close by other means If the cavity is an apical one or in the posterior segment of an upper lobe, thoracoplasty will have to be balanced against resection as the treatment of choice and the considerations already outlined will be borne in mind Resection is also desirable where a lung has been destroyed by tuberculosis, as long as there is no disease in the other lung or this has already been stabilized by chemotherapy. The patient's capacity to withstand an operation must also be assessed, and it must be remembered that the risk of the operation must be balanced against the risk of not doing the operation If the maximum breathing capacity is less than 40 litres a minute, operation carries an added risk. In some patients a considerable operative risk should be accepted when it is almost certain that the patient will die if no operation is carried out If tuberculous bronchitis has resulted in marked stenosis of a bronchus, particularly in the lower lobe, the patient is liable to recurrent attacks of secondary infection, and this may be an indication for resection Cavities in the lower lobe are not susceptible to treatment with thoracoplasty. If chemotherapy, perhaps supplemented by a pneumoperitoneum, has been unsuccessful in closing the cavity, resection should be considered.

Whether non-cavitated tuberculous disease should be resected is a question to which there is not yet a certain answer Formerly large solid lesions or extensive disease without cavitation were resected as a prophylactic measure, as it was felt that these lesions carried a high risk of relapse. With the success of long-term chemotherapy and the low relapse-rate at the present time in patients treated in this way, some physicians have now lost their enthusiasm for surgical treatment.

Other Operations.—There are a number of other operations which have been designed for the treatment of pulmonary tuberculosis. In extrapleural pneumothorax a space is created in the extrapleural tissues at the apex and this is kept refilled with air Tuberculous or other infection of the space was not uncommon, the results were not very good and the operation has now been largely abandoned. Similar operations in which various foreign bodies, usually plastics in the form of balls or packs, have been introduced into the extrapleural space have also had their vogue and are still used by some surgeons. They are, however, becoming less popular.

Post-operative Care.—The care of patients who have undergone operation for tuberculosis need not be detailed here. It is general practice to keep the

patient in bed for one to three months and then to rehabilitate him gradually. The duration of post-operative chemotherapy will depend partly on how long chemotherapy has been given before operation and partly on the amount of residual disease. Three months' chemotherapy after operation should be a minimum, and in many cases six months or more may be indicated. Most patients have remarkably little residual disability from their operation and can undertake most ordinary work, apart perhaps from heavy labouring.

Rehabilitation.—Rehabilitation of a patient with pulmonary tuberculosis is very much less difficult than formerly. The patient is often off work for less than a year and his previous employment is often available to him. Although it is probably undesirable for patients with severe disease to return to posts involving heavy physical work, it is now unnecessary to subject patients to the years of semi-vegetable existence which used to be their lot If the work to which the patient must return is likely to involve strain, this should be an

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may occur at any age. Formerly it was found that between 15 and 30 per cent. of patients with tuberculous pleural effusion would later develop other post-primary forms of tuberculosis. Although no controlled trials have been published, experience suggests that the pleural effusion is absorbed more quickly as the result of adequate chemotherapy and that the incidence of relapse with post-primary pulmonary tuberculosis is greatly lowered. An effective method of using chemotherapy in pleural effusion is to aspirate the effusion as completely as possible and insert 3 g. of streptomycin sulphate in 10 to 12 ml. of distilled water into the pleural space. This is repeated every third day until no further liquid is obtained. Usually not more than three aspirations are necessary, after which no further fluid reaccumulates. It is unnecessary to administer intramuscular streptomycin during this period, as the streptomycin is well absorbed from the pleural cavity, but isoniazid 0·1 g. twice a day by the mouth should be given. When no further fluid can be obtained a daily intramuscular injection of streptomycin is substituted for the pleural injection, isoniazid being continued as before. Breathing exercises are then instituted to encourage the return of full movement of the diaphragm. Chemotherapy should be continued for a year, although PAS and isoniazid, in doses outlined above, can be substituted for streptomycin after the patient leaves hospital.

It is usual to keep the patient in bed until the sedimentation rate is normal. He can then slowly resume his activities over a few weeks and return to his normal work. There is no evidence that a prolonged "sanatorium régime" reduces the rate of relapse from post-primary pulmonary tuberculosis. But it is most important that the patient should be kept under observation for at least five years. He should have a chest radiograph at least three-monthly for the first two years and thereafter six-monthly for the next three years.

OTHER FORMS OF TUBERCULOSIS

In general, the hospital treatment and chemotherapy of the other forms of tuberculosis mentioned below are similar to those of pulmonary tuberculosis. In all forms it is advisable to continue chemotherapy for at least a year in order to prevent recurrence in the local site or elsewhere. It must always be remembered that active tuberculosis may be present in more than one site and careful examination is imperative. All patients should have a chest radiograph at regular intervals and should have their urine frequently examined. The epididymes should always be palpated initially and thereafter included in routine re-examination.

Tuberculous Laryngitis.—With the early use of chemotherapy this is now comparatively rare. *It responds rapidly to chemotherapy, the patient losing his* symptoms usually within a few days. It may, however, take a few weeks or a month or two before the appearance of the larynx returns to normal.

Tuberculous Bronchitis.—Tuberculous bronchitis responds so well to chemotherapy that less direct interest is being taken in its bronchoscopic diagnosis. When bronchitis has been severe the most important residuum is bronchial stenosis with fibrous stricture. Especially when a lower or middle lobe bronchus is affected, there may be recurrent secondary infection requiring resection of the affected portion of the lung.

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underlying tuberculosis. In the early stages it may be possible to deal with the [illegible]

to chemotherapy, though sometimes it is later complicated by intestinal obstruction due to adhesions. The patient will require two to three months' bed-rest, but should continue chemotherapy for at least a year. Tuberculous enteritis and ileo-cæcal tuberculosis also respond well and will require a similar programme of treatment. However, in tuberculous enteritis there is usually severe pulmonary disease, the treatment of which will dominate the picture.

Superficial Tuberculous Lymphadenitis.—The treatment of tuberculous lymphadenitis with drugs is not yet entirely satisfactory Some cases appear to respond excellently, but in others the glands break down in spite of chemotherapy If there is a large mass of glands it is best to advise bed-rest in hospital in the first place. If there is fluctuation, the pus should be aspirated and 0 5 to 1 g. of streptomycin in 2 to 3 ml of distilled water should be injected locally The volume injected should always be less than that which has been removed and the injection should be made from the top of the gland to avoid development of a sinus The injection can be repeated two to three times a week. At the same time intramuscular streptomycin and oral isoniazid should be given in the usual doses. The situation should be reassessed in six to eight weeks. In many cases the glands will by then be diminishing in size and the progress will be quite satisfactory If no progress has been made within this period, it probably saves the patient time to have the glands, or at least the larger glands, removed surgically. The patient should be kept in hospital for two to three weeks after the operation, chemotherapy being continued He can then be discharged on treatment with PAS and isoniazid It is wise to continue chemotherapy for a total of at least a year. In patients so treated the relapse rate is low.

If surgery has proved unnecessary, chemotherapy should be continued for a similar period Once the glands are subsiding satisfactorily it is possible to discharge the patient from hospital. If his employment does not involve heavy physical effort he will probably be fit to start work within a few weeks of discharge.

In severe cases an attempt has recently been made to avoid skin sinuses or the necessity for operation by combining cortisone with anti-tuberculous [illegible]

two to three months, chemotherapy being given along the lines already indicated.

Genito-urinary Tuberculosis.—Genito-urinary tuberculosis should be [illegible]

there has been severe ulcerative damage before the start of chemotherapy the ultimate bladder capacity may be small and the patient may suffer from

permanent frequency.
likely if streptomycin i
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lesions is considerably more difficult. For patients with bacilluria without demonstrable alteration in the pyelogram, prolonged chemotherapy for a year to eighteen months is all that is required. At the other extreme, if a patient's kidney is severely damaged with extensive cavitation, nephrectomy should be advised. It is best to postpone this operation for three to four months so that the patient's bacterial population may be considerably reduced before the operation is undertaken On the other hand, the patient's condition is often very gre[...] improved once the damaged kidney has been removed, so there is little to [...] of cases in [...] if both kidneys are involved, requires great judgment and experience. In general, the present tendency is to be more conservative regarding surgery in view of [...] If there is any doubt, the

at least a year and in any cases in which the renal damage is at all severe two years should be the minimum period of treatment. When treatment has ceased, the patient should be carefully assessed at intervals to detect a relapse at the earliest moment However, with prolonged chemotherapy, the relapse rate at present is low, though insufficient time has elapsed to assess the long-term results.

Tuberculous salpingitis in the female usually responds excellently to chemotherapy Even large masses may shrink in the most dramatic manner. Surgery should never be undertaken until chemotherapy has been given a thorough trial. Tuberculous endometritis also responds satisfactorily to chemotherapy. Unfortunately fertility is seldom restored. As in other conditions, the chemotherapy should be continued for one to two years

Tuberculosis of Bones and Joints.—For the surgical management of bone and joint tuberculosis orthopædic textbooks should be consulted. In general, the patients are best treated in tuberculosis hospitals with close co-operation between physician and surgeon. It must always be remembered that tuberculosis is a generalized disease and that other organs may well be involved. Anti-tuberculous chemotherapy will greatly shorten the patient's stay in hospital, avoid some surgical procedures and allow other forms of surgery to be undertaken at a much earlier time. It is frequently possible to evacuate abscesses, remove sequestra and suture the wound without subsequent trouble. Tuberculosis confined to the synovia, particularly of the knee, responds excellently to chemotherapy and operation may often be avoided. Stabilizing operations may be needed for tuberculosis of the vertebræ and of the hip. Chemotherapy should be continued during the whole of the patient's stay in hospital and throughout the period of healing, often for eighteen months to two years.

Tuberculosis of the Eye.—A number of diseases of the eye, such as choroiditis or iritis, are thought sometimes to be due to a form of hypersensitivity to the tubercle bacillus. A diagnosis may have to be based on such indirect evidence as a marked skin sensitivity to tuberculin or an abnormality in a chest film. Such lesions appear to respond to prolonged chemotherapy,

but it is difficult to say how far the improvement may not be the result of a natural remission. It is usually unnecessary to admit the patient to hospital, and PAS and isoniazid may be given at home Local cortisone treatment, at the same time as the anti-tuberculous chemotherapy, may be of value.

Tuberculosis of the Skin.—Tuberculosis of the skin is now uncommon The introduction of calciferol (see p. 128) has revolutionized the treatment of lupus vulgaris, but excellent results have also been obtained with isoniazid. This has often been given alone, but it is probably safer to give it in one of the combinations already mentioned (see p. 128) It is wise to continue chemotherapy for at least six months after the lesions have become quiescent. The results in tuberculide lesions are said to be less impressive

SYMPTOMATIC TREATMENT

Symptomatic treatment, which used to bulk large in the management of tuberculosis, is now much less important With anti-tuberculous chemotherapy

few weeks

Hæmoptysis is a clinical feature which is alarming to both the patient and the doctor. Fatal hæmoptyses do occasionally occur, but they usually kill the patient within a few seconds Most hæmoptyses in which there is time for treatment are unlikely to be serious The first step is to reassure the patient, who is not unnaturally alarmed It can be pointed out to him that he would not be particularly worried were the blood coming from his nose and that he

MARRIAGE AND PREGNANCY

In advising a patient with tuberculosis about marriage, many factors should be taken into account The chief of these are the social conditions of the patient and the severity of the previous disease It must be remembered that a prolonged engagement is in itself a strain. It is now much less important to postpone marriage because of risk of relapse The additional strain can be met by prolonging the period of chemotherapy. In most cases it is reasonable for the patient to marry when the disease has been quiescent for a year, as indicated

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during the
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years. But it is important to take everything into account. If the patient is over the age of thirty, and especially if she has had no previous children, the physician will be less inclined to advise delay. If she is already having chemotherapy, pregnancy will be an indication to prolong its duration. If chemotherapy has

drugs have any deleterious effect on the fœtus.

If the patient's disease has only recently become quiescent, it is important to arrange for rest over the period of parturition. It is wise to admit the patient to hospital two to four weeks before the expected day of delivery and to keep her in hospital for four to six weeks afterwards. This will cover the period during which the infant is having BCG. Until the disease has been quiescent for at least three to four

Therapeutic

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in which the therapeutic programme might require surgery about the time of parturition. It will have to be more seriously considered if the patient's tubercle bacilli are drug-resistant and the physician is anxious not to add in any way to the patient's burdens. There is little point in carrying out therapeutic abortion after the end of the third month of pregnancy. After that the operation involves as much strain as parturition.

J. Crofton.

COMMON DISEASES OF THE SKIN

INTRODUCTION

THE SITUATION of the skin renders it vulnerable to physical, chemical and bacterial irritants acting from the outside. In this respect it is similar to the mucous membranes, but differs from most other organs of the body. Irritants are the cause of many skin diseases, while others result from causes which produce their effect from within and reach the skin via the blood stream. Yet another group of diseases of the skin is due to derangement in the growth or metabolism of one or other of its various cellular components.

The interference with skin function which is bound to result from an extensive eruption does not necessarily produce any grave systemic symptoms or upset in general health such as accompanies the derangement of function associated with disease of other organs. Nevertheless, extensive destruction of the skin surface may prove fatal. Modification and control of function plays a great part in the treatment of disease of certain organs other than the skin, but variation in the function of the skin can only be produced to a limited extent, and the employment of methods calculated to produce such changes is not rewarded with much success in the treatment of skin diseases. From what has been said it may be gathered that the treatment of skin disease solely by internal methods, while often desirable on theoretical grounds, is not entirely satisfactory from the practical point of view.

Before discussing separately the treatment of the common skin diseases, it will be an advantage first of all to give a detailed description of the technique employed in the application of external remedies, for this is a subject of particular importance.

LOCAL TREATMENT

Generally speaking, the use of soap and water is indicated in the treatment of all skin diseases for general cleanliness, and for assisting the removal of surface therapeutic applications and the products of the disease, such as crusting and scaling. Washing may cause a temporary increase in itching and burning, but this can be ignored in the majority of cases as it is generally transient. Occasionally, however, very sensitive inflamed skins will not tolerate the use of soap and water because the reaction which is produced does not subside rapidly, and the condition is aggravated. In such cases cleansing has to be carried out exclusively with olive oil, or peach kernel oil. It may also be necessary to use these oils prior to washing with soap and water in order to soften crusts or therapeutic agents which have been applied to the skin. Occasionally patients complain of a feeling of irritation and dryness after the application of olive oil, but this is rarely a serious drawback to its use.

Baths may be given in all skin diseases, but may on occasion cause irritation in the same way as when soap and water are used for washing purposes. The temperature of the bath should not be more than 100° F., and a patient may soak in it for fifteen to twenty minutes. A number of drugs may be added to the bath, but it is very doubtful if such medicated baths have any real value, although

patients with an extensively inflamed skin may find a starch bath more comfortable than an ordinary one. The following are the common agents which may be added to a bath of approximately 180 litres (40 gal.).

Starch bath: 0 25 kg. ($\frac{1}{2}$ lb.) of starch is first mixed with cold water in a basin to make a paste, and the bath is filled by allowing the hot water to run into the basin and overflow from it into the bath

Potassium permanganate bath: Potassium permanganate crystals are added in sufficient quantity to make the water a bright pink colour, and the patient is immersed for ten minutes before soap is used.

Bran bath: 1 8 kg. (4 lb.) of bran contained in a muslin bag are placed in the bath, which is then filled by allowing the tap to run on to the bag.

Sulphur bath: 60 to 120 g. (2 to 4 oz) of sulphurated potash are put in the bath prior to filling.

The cleaning of the bath contaminated by medicaments added to the water, or by pastes or exudations from the patient's skin, is a matter of practical importance. Sulphur, potassium permanganate, tar, chrysarobin, silver nitrate and the aniline dyes will stain a bath if it is not cleaned immediately and thoroughly after use. For a greasy bath, Vim, Brooke's soap or paraffin may be used; for chrysarobin, a mixture of paraffin and bath-brick; for the aniline dyes, turpentine or methylated spirit.

Powders.—For ordinary purposes starch, talc or kaolin, used either singly or mixed in equal parts, form suitable bland powders which can be dusted on as a protective and cooling application to an inflamed surface, e.g. in erythemas, in dry scaly dermatitis and in herpes zoster. They are only useful when the eruption is of a dry nature, because if there is any discharge the powder cakes and acts as a mechanical irritant Drugs such as boric acid, salicylic acid and [illegible]

[illegible]

having the consistence of a paste, and these watery pastes are sometimes useful in acutely inflamed erythematous eruptions, particularly in acute sunburn.

Poultices.—The only poultice which is really efficacious and of outstanding value in the treatment of skin diseases is the starch poultice. It is made in the following way, using either wheaten or maize starch:

To make a starch poultice for the scalp, four tablespoonfuls of starch, one teaspoonful of boracic and one pint of water are required. Double this amount is needed for a poultice for the hand and arm. The starch is put into a basin and the boracic, after being crushed to a powder, is added to it It is then mixed with cold water until it forms a thick cream. Boiling water is added until the diluted cream sets into a jelly. During this addition the mixture is stirred continuously with a wooden spoon. The jelly so obtained is beaten with the spoon for a few minutes until the starch is smooth, and it is then left until quite cold.

The cold jelly is spread in a layer about $\frac{3}{4}$ in. thick on a piece of strong [illegible]

When a whole limb is being treated with starch poultices, two should be made and applied to the upper and under surfaces so as to overlap at the sides.

The ordinary washing starches do not produce as good a jelly as do wheaten, maize, or even potato starches If desired, the initial paste may be made with 1 per cent. aqueous solution of gentian violet or 1 : 1,000 aqueous solution of acriflavine instead of ordinary water A charcoal starch poultice may be obtained by adding 4 to 8 g of charcoal to the cold-water paste before the addition of boiling water.

The application of starch poultices is a universally safe treatment for all exudative forms of skin disease, and with ingenuity they can be applied and retained in position on any part of the body Their disadvantage is their weight and sometimes the feeling of clamminess which they produce. When starch poultices are being used it may be necessary to keep the patient in bed in order to allow applications to be made and to be kept in position. It is particularly important to avoid a hard edge of linen or calico coming into contact with the eruption. The poultices should lift off easily and leave, practically speaking, no starch adherent to the skin surface They absorb exudate into their substance and thus reduce the chance of the dressing causing a spread of infection by the retention of discharges, or by their extension to adjacent areas as is liable to happen with ordinary occlusive wet dressings Starch poultices are difficult to make, and if not made properly they may either be lumpy, too moist, or may dry to a cement-like consistency after an hour or two, and in consequence do considerable harm. They should be renewed every four or five hours, and as good poultices come cleanly off the skin, washing the part once daily is all that is required In this way a minimum of interference with an inflamed surface is ensured

Lotions.—Lotions may contain medicinal substances either in solution or in suspension. A lotion commonly employed is one containing glycerin and an inert powder in addition to the medicinal substances dissolved or in suspension in the fluid vehicle They are usually made up with water, but spirit may be added to the water, and some lotions are entirely spirituous Lotions may be applied either by dabbing or painting them on with a pledget of cotton-wool or a brush, or by applying strips of calico or linen soaked with the lotion which are then covered with some occlusive material such as oiled silk or jaconet If the surface to be treated is extensive, the lotion should be brought to blood heat before use. A powdery lotion when painted or applied to the surface has a cooling effect due to the evaporation of water, and thereafter a thin layer of powder is left on the skin surface which remains adherent on account of the glycerin contained in the lotion

Lotions are useful because they are easy to apply, are clean and in virtue of their cooling effect are efficient in allaying itch They are used in inflammation of the skin in all its forms, and they may be applied, even as occlusive dressings, to large areas of the body surface Lotions are removed by gentle washing with soap and water, if necessary after a preliminary softening with olive oil Should some of the lotion become adherent to an irritable surface it should be allowed to remain, because vigorous rubbing will only further irritate and inflame the area

Ointments and Pastes.—Ointment bases may be either animal fats or mineral oils of suitable consistence, and these substances may be used alone or in the form of water in oil or oil in water emulsions. An example of the former

is unguentum aqua rosæ, and the latter may be compounded by adding an emulsifying agent such as lanette wax s.x. to a mixture of the greasy base and water:

Lanette Wax . . .	30 G. (1 oz.)
Liquid Paraffin	
Water	of each 30 ml. (1 fl oz.)

For practical purposes, lard, hydrous wool fat and soft paraffin are all the bases which are required. Ointments are used as a vehicle for the [illegible] is carried out, the palm of the hand should be used in preference to the finger tips, the inunction being performed with steady even pressure and in a unidirectional manner if the part is hairy

An ointment may be stiffened by the addition of an inert powder such as zinc oxide or starch to give it the consistence of a paste. The same medicinal substances may be incorporated in pastes as in ointments. Pastes cannot easily be rubbed in unless they are very thin, that is to say, containing not more than 10 to 15 per cent. of powder; if they are stiffer they must be applied spread on strips of calico or linen varying in width from ½ in. for the fingers to 3 in. for the limbs. If the trunk has to be dressed, material is shaped to fit, overlapping the shoulders and sides and cut to clear the axillæ. For the head and face a mask is used, and this should always cover the head, even when the face only is being treated. The material is pinned at the sides of the head and neck and kept in position with a bandage. A mask which only covers the face and is not carried over the head will invariably slip out of position and be uncomfortable. Pastes cannot conveniently be applied to surfaces covered with hair, and should their application be necessary to such areas the part must be shaved. Pastes are, generally speaking, more useful than ointments, although they are more difficult to apply. Being stiffer in consistence than ointments, they lend more support to the area to which they are applied, and a certain amount of exudate may penetrate into the interstices of the paste. Although it cannot be demonstrated that a paste is capable of absorbing water or serum, there is no doubt that pastes [illegible] applied to exudative lesions with benefit, whereas ointments are unsuit- [illegible]

emulsion is used as a base it will be unnecessary to use oil as a preliminary cleansing agent as the emulsion is easily removed by soap and water alone.

In this country from 15 to 20 per cent of inert powder added to an ointment base will give a paste which is easily applied and easily removed. In warmer climates it may be necessary to increase the quantity of powder in pastes for general use, and in certain circumstances a larger amount of powder may be required even in colder climates.

The amount of ointment or paste required for a single dressing of different areas in an adult is approximately as follows when spreads are used: (1) face, head and neck, 60 g. (2 oz.); (2) hand, fingers and whole arm, 60 g. (2 oz.);

(3) back or front of trunk, 60 g. (2 oz.); (4) entire skin surface, 0·45 to 0 7 kg. (1 to 1½ lb.).

Paints.—Some antiseptics, and particularly the aniline dyes, are applied to the skin in the form of paints which dry on the surface These drugs may be dissolved in water, in spirit, or applied undiluted. Paints in common use are: (1) the aniline dyes in watery or spirituous solution; (2) ichthammol and silver nitrate, either alone or combined, in watery solution; (3) silver nitrate dissolved in spirit of nitrous ether Crude gasworks tar in the form of a thin varnish is applied as a paint which, after five minutes, is powdered with talc or starch. This preparation dries in about fifteen to twenty minutes and is allowed to remain on the skin for from twenty-four to forty-eight hours. It may then

produced by spirit.

Permanent fixed dressings are not of great value in dermatology except in artefact dermatitis and as a final dressing in varicose dermatitis. The preparation which is least likely to irritate an inflamed or recently inflamed skin is Unna's ichthyol zinc gelatin

CHOICE OF TREATMENT

The choice of drug and its strength depends entirely on the type and stage of the eruption which is under treatment. Generally speaking, substances such as ichthammol, ammoniated mercury, boric acid and tar may be used in concentrations of ½ to 1 per cent. in the treatment of acutely inflamed conditions. If much scaling is present, drugs which have a solvent action on scales are

lkaline caustics may be necessary.
the treatment of skin diseases requires

medical may be applied.

FORMULÆ FOR COMMON LOCAL APPLICATIONS

Baths (see preceding text).

Lotions

Calamine—

Boric Acid		5
Calamine		15
Zinc Oxide		15
Glycerin		10
Water	to	200

and it might be thought that it would be definitely contra-indicated in sycosis.

the reason why the inflamed skin can tolerate crude tar is that the tendency to follicular infection has subsided and the actual lesion which benefits from the tar

in early cases.

Epilation with X-rays is necessary in a large percentage of cases affecting the

but when the hair commences to grow again a small area of pustulation may recur and spread to involve the whole of the area originally affected. Such small areas to the

d one,

PARASITIC INFECTIONS

RINGWORM

are due to its situation in the skin, its normal resistance to antiseptics and the susceptibility of the skin—particularly the inflamed skin—to chemical irritation.

Ringworm of the Body.—When a fungus infects the non-hairy non-flexural surfaces its destruction is a fairly easy matter. With the exception of the palms and soles, where the stratum corneum is thick, the fungus is situated on and very close to the surface, is easily accessible to antiseptics and the area can readily be cleansed. In tinea corporis, therefore, repeated painting at daily intervals or every second day with a 2½ per cent. tincture of iodine or basic

Ringworm of the Scalp.—This presents a much more difficult problem because the fungus is present inside and surrounding the hair shaft in its

intrafollicular portion, and in this situation it is exceedingly difficult for antiseptics to reach it. It is therefore necessary to epilate the scalp either by means of X-rays or thallium in order to get rid of the infected hairs, and so to permit the entrance of antiseptics into the follicles. The technique of X-ray treatment [illegible]

which must be carried out with scrupulous attention to detail, because thallium is a dangerous drug producing severe constitutional symptoms and possibly death if wrongly used.

[illegible]

afterwards in about 30 per cent of children. This takes the form of temporary lassitude associated with rheumatic pains in the legs. The symptoms last only for a few days From seventeen to twenty-one days after the administration of the epilating dose the hair commences to loosen and can be plucked out painlessly all over the scalp; the eyebrows are not affected. Compared with X-ray epilation, the fall of hair due to thallium occurs earlier, is less complete [illegible]

Thallium should not be administered to a child weighing over 30 kg. unless in very special circumstances, when a dose may be given to children weighing up [illegible]

The treatment of ringworm of the scalp would therefore be as follows:

After a diagnosis has been made, the hair is clipped short all over the scalp, and this may reveal the presence of hitherto unsuspected patches of disease. The scalp is then treated twice daily with a 10 per cent. sulphur ointment, and [illegible]

washing are then both stopped altogether for a period of three weeks, at the end of which time the scalp is examined. If any fungus has escaped destruction by the an[illegible]
treatm[illegible]
child [illegible]
daily, [illegible]
for the presence of disease, and, of course, an infected child must not attend school.

The infiltrated lesions known as kerion, which are produced by infection with virulent fungi derived from animals, do not require epilation because they

cure themselves in from three to four months' time by the production of a natural immunity to the fungus. All that is necessary in treatment is the relief of pain by starch poultices or wet dressings in the early stages, and the limitation of secondary infection by means of a 1 per cent. ammoniated mercury paste when the phase of infiltration is subsiding. Similar measures are used for ringworm of the beard, a condition which must be differentiated from sycosis, and one which, like kerion, runs a self-limiting course calling only for palliative treatment

Ringworm of the Body Folds (Epidermophytosis). Infection with the

digital areas to involve the soles of the feet, and the palms of the hands may also become affected. A great variety of antiseptics have been used in the treatment of this particular type of fungus infection, but while many are efficient it cannot be said that any one of them is outstanding. Tincture of iodine in strengths from 0·5 to 5 per cent. may be used according to the tolerance of the individual skin, and swabbing the area with a 3 to 5 per cent. solution of silver nitrate in spirits of nitrous ether is a clean and useful method. If there is marked secondary infection with pyogenic organisms, a 2 per cent. solution of gentian violet may be used in the early stages. When the condition has reached a dry scaly stage, an ointment containing 6 per cent. benzoic acid and 3 per cent. salicylic acid should be used in preference to lotions. Certain fatty acids, normally present [illegible]

(1) *undecylenic acid, grade AA, 5 per cent., zinc undecylenate 18 per cent.,* propylene glycol, N.F., 10 per cent., carbowax 1500, 19 per cent., carbowax 4000, 29 6 per cent , distilled water to 100 per cent. ;

(2) zinc undecylenate 20 per cent., purified talc 78 per cent., undecylenic acid, grade AA, 2 per cent.

The powder is used in infections of the feet and groins. In monilial vulvo-vaginitis the undecylenic ointment formula should be diluted with equal parts of "K.Y." jelly. X-ray treatment is useful in cases which do not respond to these measures.

Should the fungus produce an intense inflammation of the skin, the more vigorous remedies may have to be withheld for the time being. Soothing applications such as starch poultices or wet dressings of boric acid solution or a solution of 10 per cent. ichthammol in water should be used until the acute inflammation—which is often associated with secondary pyogenic infection—has subsided. In the acute vesicular pompholyx-like eruptions which affect the soles, palms and the sides of the fingers, wet dressings of ½ per cent. silver nitrate in water are most beneficial. They are applied twice daily for three or four days, and usually cause rapid desiccation of the vesicles and prevent the appearance of fresh ones At the end of that time a 1 per cent. ichthammol paste is used and finally the benzoic and salicylic vaseline should be applied.

Infections of the feet are extremely stubborn and resistant to treatment, and it is doubtful whether the infection can ever be completely eradicated from this area. When the condition seems to be in abeyance the individual should be advised to apply an antiseptic, such as tincture of iodine, periodically to the affected areas.

wearing apparel, and especially all the articles with which the infected person comes into contact in the bathroom, i e. bath mat, floor, etc. In a private house there is no need to anticipate a spread of the infection provided reasonable precautions are taken. The disease is usually acquired from the floor of dressing-rooms, swimming baths, Turkish baths, *plages* and, in infection of the groins, from lavatory seats. When an object or room has once become infected, it is often a difficult matter to secure complete destruction of the parasite even by the use of strong disinfecting measures. The condition is so prevalent that no

occur as an isolated event, or the nails may become infected from already existing lesions on other parts of the body. The difficulties in treatment are

being cured or disappearing spontaneously Infection of other parts of the body from an infected nail, although a possibility, is uncommon, and experience shows that an individual suffering from ringworm of the nails need not be considered a grave source of danger to others.

SCABIES

At the present time 5 per cent. sulphur ointment or 25 per cent. emulsion of benzyl benzoate are the two most satisfactory and certain methods of treatment. The former is the cheaper, but takes longer; it is the more suitable of the two for severe cases. The latter is expensive but rapid and clean, and is sufficiently certain in cases of medium severity. Benzyl benzoate treatment is

daily for two or three days, and while clean underwear is worn twelve hours after the last treatment, the bath may be postponed for a further period of two days.

Sulphur treatment is carried out as follows · The patient steeps in a bath for

twenty minutes, lathers all over with soft soap and scrubs the affected areas with a soft nailbrush to open up as far as possible the burrows of the acarus. Thereafter a 5 per cent. sulphur ointment is rubbed in thoroughly all over the body with the exception of the head. The inunction is repeated at intervals of twelve hours, till six applications have been made. If convenient the legs, feet, arms and hands may then be bandaged, thereby enhancing the lethal effect on the parasite. Twelve hours after the last treatment a bath is given, clean underwear worn and the bedding disinfected. In mild cases four, or in urgent circumstances two inunctions only, may be given.

If there is a severe complicating impetigo it should be treated in the usual way for a few days before sulphur ointment treatment is begun. Confinement to bed is essential in all infected cases, for although the parasitic element is eliminated in three days, the entire treatment of a severely infected case may cover a period of four to six weeks.

The patient is usually free from itch after the first or second inunction, and he remains so unless the sulphur irritates his skin. A few patients develop a mild dermatitis after the six applications, but this yields readily to a calamine or lead and zinc lotion used for a few days after cessation of the sulphur treatment. Recurrence of the irritation in a week to ten days after treatment has been completed means a recurrence of the disease, either due to inefficient treatment or to reinfection.

The efficiency of sulphur has been adversely criticized because of the occasional development of sulphur dermatitis. This complication is, however, due less to the efficient intensive use of a 5 per cent. sulphur ointment over a period of three days than to the inadequate intermittent use of such an ointment over a prolonged period.

It is important to examine and, if necessary, to treat all contacts and also to make sure that the infected bedding has been adequately disinfected, although it must be admitted that fomites do not play an important part in the transmission of the disease. The search for infected contacts and the proper handling of fomites may throw considerable strain on the public health services.

PEDICULOSIS

Pediculosis Capitis.—The prevalence of pediculosis capitis is greater than is generally realized. It may be treated by means of common paraffin oil in the following way. The forehead, ears and neck are first protected with zinc ointment, then, with no preliminary washing, the hair and scalp are soaked with

application has been removed, the scalp is washed. The adult parasites are readily killed by this method, and the nits can later be removed by combing with a small-tooth comb which has been dipped in weak acetic acid. Oil of sassafras, xylol, and 1 in 40 aqueous solution of carbolic acid may be used in the same way as paraffin oil.

Recently it has been found that a mixture containing 25 per cent. lauryl thiocyanate in refined liquid paraffin (Lethane Oil) is capable of destroying the parasites, and it is a more pleasant method of treatment than those hitherto in use. The mixture is rubbed into the scalp once only, and the scalp is left

unwashed for ten days, during which time the lauryl thiocyanate exerts its action on the pediculi and nits.

If the infection is severe, the nits numerous and an extensive impetigo present, it may be necessary as a preliminary measure to cut the hair, and subsequently shave the scalp (see p 151) No matter how impetiginous the

the glands.

Dicophane (DDT) (see p. 232) is a parasiticide which is lethal to all varieties of pediculus and many other parasites which infest man, animals and plants It can be applied as an e

most effective remedy

its ovicidal action is weal

persists on the skin and hair and so kills the larvæ as they hatch out. Dicophane

axillæ, eyebrows and lids can be infected with this parasite.

Pediculosis Corporis.—This is treated in the same manner as scabies, and a bath followed by one or two inunctions of sulphur ointment, and disinfection of the underwear, is usually sufficient to eradicate the infection. To prevent re-infestation the undergarments can be dusted with 5 per cent dicophane powder in talc.

Pediculosis pubis and corporis are apt to occur in sudden widespread epidemics when conditions lead to overcrowding. Compared with scabies the spread of this type of parasitism is more rapid, but when bathing and laundry facilities become available its control is a simple matter These differences are due to the greater inherent mobility of the louse as compared with the acarus, and to the fact that it dwells on the clothing and on the skin surface and not in the skin substance as does the acarus. In crowded communities parasitism is the most common predisposing factor in the development of boils.

ACNE

The development of acne is ultimately dependent on the functions of the endocrine glands It may be due to an excessive secretion of androgens, and may indeed be produced by testosterone treatment, or it may result from a relative upset in the androgen/œstrogen ratio rather than to a disturbance in their absolute amounts Nevertheless, the main treatment of the condition is essentially local. Overactivity of the sebaceous glands seems to be the important local predisposing factor in the development of the condition It results in the formation of the comedones, fosters the growth of pyogenic organisms and so predisposes to pustule formation.

(4) internal treatment for the reduction of the functional activity of the sebaceous glands. Frequent swabbing of the affected area with ether or surgical spirit may

be advised to remove the surface grease. Once daily, preferably at night, the face is very thoroughly washed with hot water and sulphur soap and the lather massaged into the skin for a few minutes. The lather is then removed, the face dried gently, and thereafter the following lotion dabbed on:

℞	Zinc Sulphate . . .	4 g. (1 dr.)
	Sulphurated Potash .	4 g. (1 dr.)
	Water . . . to	120 ml. (fl. oz. 4)

The lotion leaves a powder on the skin and this is allowed to remain on overnight and is washed off in the morning. After a week or ten days of this treatment the following peeling paste may be used:

℞	Betanaphthol . . .	2 g.
	Precipitated Sulphur . . .	4 g.
	Balsam of Peru . . .	15 g.
	Soft Paraffin . . . to	30 g.

The paste is smeared on the affected areas at night and removed in the morning with olive oil. Immediately after its application it causes a good deal of nipping and burning, which lasts for about a quarter of an hour and then subsides. The effect of the paste is that of an antiseptic and counter-irritant, and it causes the skin to become slightly inflamed and subsequently to peel. This desquamating effect clears the mouths of the follicles, thus facilitating the removal of blackheads and dammed-up sebaceous material, and, in virtue of the antiseptic action of the paste, surface infection is reduced. It is not as a rule

better to stop all active local treatment and merely to use mild applications such as calamine lotion It may be said that X-ray therapy is essential at some stage in the treatment of all but the mildest cases of acne. X-rays are best administered

producing a beneficial action on the whole of the exposed surface.

General internal measures consist of the administration of iron and the reduction of carbohydrate intake, especially the actual sugar content of the diet.

The administration of œstrogens (stilbœstrol 1 mg. daily) is followed by improvement in a proportion of cases in *both* sexes. *Such treatment must be* employed with caution in the adolescent male, and in the female it should be given only during the second half of the intermenstrual period.

Large doses of vitamin A may have a beneficial action in chronic deep-seated indurated eruptions.

It is also necessary to see that the scalp is washed regularly, because it is invariably greasy and often scaly. Organismal contamination in these circum-

stances is abundant, and the chance of pustulation due to infection from the scalp is increased.

ROSACEA

Rosacea is almost always associated with one or more of the following conditions: a certain amount of seborrhœa of the face; seborrhœa and pityriasis of the scalp; a mild degree of indigestion; symptoms indicating slight ovarian dysfunction. The local predisposing factors are a marked tendency to capillary flushing, very open pores and an increased virulence in the organisms which normally contaminate the surface Treatment may therefore have to be directed towards the correction of one or all of these contributing causes A sulpho-calamine lotion is probably the best local application, and it may be helpful to alternate it day about with either a 1 per cent. sulphur paste or a 1 per cent. ichthammol paste. A peeling paste used in the same way as in acne may be helpful in some cases In addition to daily treatment, weekly fractional doses

each of salicylic acid and resorcinol and 4 ml. (1 fl dr) of castor oil in 160 ml. (6 fl. oz.) of spirit.

The diet should be plain, all spicy foods should be eliminated from it, and the patient should be instructed to allow all hot fluids to become cool before they are ingested Some patients will be found to improve if an alkali is given after their main meals, and in others the administration of dilute hydrochloric acid is helpful.

Vaccine therapy is of little value in rosacea even when pustulation is marked.

If rosacea is treated in its early stages, the affected skin will return to normal and the vascular dilatation will subside. If, however, the eruption has been

ECZEMA

Eczema is a specific type of skin reaction characterized by superficial inflammatory œdema of the epidermis associated with vesicle formation After a longer or shorter time this reaction passes through a scaly phase towards healing.

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to one or more of the drugs which are commonly used in the treatment of the disease is encountered in a number of cases. The irritant factor which has caused the eruption may continue to act for a considerable time after treatment has been instituted, and for this reason the fact that treatment has been commenced does not ensure that the eruption will from that time forward proceed towards healing. Sometimes the patient carries out the treatment prescribed in

precipitate fresh patches. Grease sensitivity is much less marked in eczema arising from internal causes When it is noted in the more acute phases of the eruption which would otherwise be treated with pastes, the use of a lead and tar lotion or ½ per cent. silver nitrate soaks may be necessary until it is in a condition deemed suitable for crude tar. Localized patches of internal eczema sometimes respond in a most satisfactory way to X-ray therapy, and in elderly people this is especially so in the chronic lichenified patches of eczema usually situated on the nape of the neck, the sacral region, the thighs or the outer aspects of the forearms.

Infantile Eczema.—*Although* a great deal of work has been done to ascertain the role of diet in the production of this type of eruption, it is only in exceptional instances that a specific protein can be legitimately incriminated as the cause. Nevertheless the condition seems to be undoubtedly associated in [illegible]

[illegible]

juice aggravates the eruption in a number of cases, and it is perhaps wise to omit it from the diet and substitute grapefruit juice, tomato juice or rose hip syrup. The daily supply of vitamins A and D should be ensured by suitable additions.

The local treatment consists in the application of tar preparations, the protection of the affected skin with bandages and the immobilization of the arms and [illegible] hands [illegible] In the [illegible] when the eruption has dried the lotion may be replaced by a 1 per cent. tar paste Crude tar may finally be used, and may be applied to large areas of skin, for it is unusual to find infants suffering from infantile eczema who are intolerant to tar.

Besnier's Prurigo.—*By this term is meant the chronic recurrent eczema* which develops in childhood and adolescence often as a sequel to infantile eczema, and which affects the flexures of the knees and elbows, the forehead and [illegible]

substances such as hair, fur, flock or feathers, but in the majority of cases the cause remains as much a mystery as the cause of the asthma which so often accompanies the skin eruption or alternates with it. A definite and striking [illegible]

Local treatment resolves itself into the application of crude tar as soon as the state of the eruption will permit, and this must be continued for a number of weeks until the maximum thinning of the affected skin has been obtained. It is hardly ever possible to bring the skin completely back to a normal texture if the disease has been present for any length of time. X-ray treatment is almost always successful in reducing the irritation and scratching, and it may be used from time to time. It must not be forgotten, however, that these patients have recurrences over a period of years, so that there is a limit to X-ray therapy on account of the cutaneous atrophy which would result if X-rays were depended on for the alleviation of every attack.

Non-specific desensitization methods may be tried in an attempt to prevent [illegible]

how rapidly an acute exacerbation will subside if the patient is admitted to hospital.

Eczema due to toxic states comparable to those found or envisaged in "rheumatism" is seen to occur with increasing frequency as age advances after middle life. The eruption may be widespread or localized, and is characterized by its extreme itchiness and tendency to exacerbations and remissions. The treatment is no different from that of Besnier's prurigo, but the response to it is much more satisfactory Free elimination is particularly beneficial, and, when the eruption is chronic and localized, X-rays are more useful than in any other form of dermatitis.

Corticotrophin and cortisone in ordinary doses are capable of suppressing the eczema reaction, irrespective of its cause Recrudescence of the reaction, often resulting in a more active condition than that prior to the commencement of treatment, will occur if the drugs are withheld prematurely In these circumstances it might obviously be necessary to continue a maintenance dose for a long period. When deciding whether or not to use these drugs in the treatment of eczema, the type of eczema to be treated, the likelihood or otherwise of its responding in a reasonable period of time to local measures, and the degree of disability which it causes, must all be carefully considered. At the present time their employment would appear to be justifiable in only a few carefully selected cases

VARICOSE ECZEMA

When varicosity of the cutaneous venules of the legs has become established, the affected area is particularly prone to develop either chemical or infective eczema. Treatment is hampered by the inefficient circulation, and the usual [illegible]

not be used when eczema accompanies ulceration.

Varicose eczema, when it heals, leaves the skin stretched, glazed and pigmented, and the recurrence which tends to take place when the patient starts to walk about can sometimes be avoided by the use of Unna's zinc ichthammol

gelatin. Sometimes it may be necessary to resort to ligation of the veins in order to prevent recurrence.

OCCUPATIONAL DERMATITIS

Eczema and simple dermatitis directly due to the individual's occupation are becoming increasingly common, and *such cases often take a very long time to heal*, even when the extent of the eruption is limited. They may be due to chemical irritation or to mechanical or caustic injury with dust or liquids, which allows infection to gain access to the deeper layers of the epidermis with the *production of an infective dermatitis* In any case, whether due to external chemical irritation or bacterial infection, internal toxic factors may commence to play a part in the production of the rash, thus prolonging its course and increasing its resistance to treatment. All these factors must be taken into account when deciding the line of treatment to be adopted. When a case has been cured, the question of returning to work and the risk of recurrence must be considered. The individual should be warned to take every possible precaution [illegible] all forms of minute [illegible] ents, [illegible] ater, should be used regularly after washing. No strong soaps or grease solvents should be used for cleansing purposes.

After an attack of occupational dermatitis has subsided it is wise to keep the individual off work for a period of one to two months in order to allow the previously inflamed skin to return as far as possible to normal and to recover from *the effects of previous long-continued inflammation. Recurrence is practically* [illegible]

GENERALIZED (EXFOLIATIVE) DERMATITIS

A number of superficial inflammatory skin eruptions, which normally occur as discrete patches, may spread to involve the entire body surface. The clinical picture so produced is referred to as generalized exfoliative dermatitis. It may result from the gradual extension of any one of the types of eczema mentioned above, in which case it assumes the characteristic features of the initial patches of the disease. Psoriasis involving the whole body is frequently mistaken for generalized exfoliative dermatitis Generalized dermatitis, which may or may not go through an exudative phase, may follow the administration of organic arsenicals, mercury, gold and other heavy metals. A similar condition may [illegible]

larly with regard to the mode of onset, and, in the leukæmic type, by a hæmatological examination.

The patient must be kept in bed for his own comfort and to permit of efficient treatment, though the danger of broncho-pneumonia has been somewhat exaggerated. The treatment has already been outlined in the preceding paragraphs dealing with the different types of eczema. Dermatitis due to the internal administration of arsenic or other heavy metals is treated in the same way as that due to external chemical irritants (see p. 162).

Generalized psoriasis is dealt with in the same way as for an individual patch of the disease. The generalized leukæmic erythrodermias are intensely itchy, and tar preparations and superficial X-ray therapy are necessary. In all these cases the dressings are extensive and time-consuming, and the disease is likely to be of long duration. From time to time the patients develop diarrhœa associated with a mild fever, and tend to become emaciated and cachectic. Appropriate measures must be taken to alleviate these symptoms.

PRURITUS

Pruritus is a sensation which is only experienced in the skin, and we are entirely ignorant of its cause. It may accompany a local pathological change which is in its essential structure similar in detail to a condition which is not associated with pruritus. Again, it is not infrequently observed that the same disease may cause intense pruritus in one patient but not in another. Itching is rarely continuous, and as a rule it comes in spasms at intervals of one to many hours, often without any apparent precipitating cause. Like the skin diseases with which it is associated, it can be profoundly influenced by external applications, so that its point of origin is presumably superficial.

Pruritus occurs most commonly in conjunction with visible pathological changes in the skin. It may, however, arise spontaneously in areas of skin having a normal appearance and texture, and it is then presumably due to the action of some internal irritant on the cutaneous nerve endings, to some irritant acting reflexly on these, or to central nervous causes.

Pruritus associated with obvious skin disease is most intense at the onset of the eruption, or just prior to an exacerbation. It is usually alleviated when the disease itself begins to subside, and the treatment of the disease is the treatment of the pruritus. Thus in parasitic, bacterial or fungus infections antiseptics are used, in inflammation due to chemical irritation protective and cooling measures usually suffice, and in conditions due to some internal poison the removal of its source combined with free elimination affords relief. It is sometimes necessary, in addition to such lines of treatment, to employ specific measures to relieve the itching, which, on account of the scratching it causes, may be a serious obstacle in the treatment of the condition responsible for it. The symptomatic treatment is limited to the application of lotions or pastes containing tar, with or without the addition of 1 per cent. phenol or menthol. Such applications are made frequently, and whenever possible the parts should be guarded from friction and changes in temperature. Exposure to X-rays is sometimes helpful. In severe cases there is no objection to the administration of sedatives of the basal hypnotic class. Morphine and its derivatives should be avoided because they have a tendency to aggravate an itch after affording initial relief. The antihistamine drugs often have a marked effect in relieving pruritus whether associated with an eruption or occurring in an otherwise normal skin. Following their successful administration, existing itching is relieved in about twenty minutes, and by repeating the dose four-hourly it may be possible to prevent the development of further attacks. This action is most certain in urticaria, but antihistamines may be equally useful in widely differing itchy eruptions. There is, however, no criterion as to whether or not they will be effective in a given case. Apart from obvious disease of the skin, generalized pruritus is

usually seen as an isolated symptom in elderly subjects due to some internal disorder or toxæmia. A careful examination is therefore necessary in every case to discover if possible any such factor, and its rectification is usually followed by disappearance of the pruritus.

The pruritus of the elderly is frequently associated with slight atrophy of the skin, and thorough lubrication with grease or creams, along with a liberal supply of vitamins and attention to elimination by kidneys and bowel, usually brings about a cure. Here, again, X-ray exposures may be given for troublesome areas, and sparking with a high-frequency current, using a flat-glass electrode, may be helpful. It is important to avoid sudden changes of skin temperature, and all garments worn next the skin must be smooth in texture. The diet must be of an easily digestible type and all spices and condiments should be forbidden. Measures should be taken to rectify any digestive errors. Hot fluids should be allowed to cool before drinking, and it is preferable to forbid alcohol. The treatment of post-menopausal pruritus vulvæ is discussed on p. 397.

is discussed on p. 508.

affected areas for any abnormality which might, by causing reflex nervous impulses, produce the itching. Psychological factors should not be overlooked

l abnormality, such as piles

In cases of pruritus ani the

f the rectum or pelvic colon

may, by causing slight peri-anal venous congestion, produce the symptom. The stools may have to be examined bacteriologically and chemically, and any abnormality rectified by dietary measures or lavage. In cases of pruritus vulvæ the patient may have to undergo a thorough gynæcological as well as a general medical examination.

The prolonged scratching associated with localized pruritus eventually leads to hypertrophy of the skin of the affected area. The local treatment of this type of pruritus is similar to that outlined above. In cases of pruritus ani and vulvæ unaccompanied by any visible skin change, the frequent application of 1 per cent. hydrocortisone acetate ointment frequently gives most satisfactory results.

Pruritus, whether localized or generalized, presents a much greater therapeutic problem when it is an isolated symptom than when it accompanies some visible cutaneous manifestation.

URTICARIA

The majority of cases of urticaria are due to intolerance to some article of diet. The eruption occurs suddenly in an acute form, and the cause is often indicated by the history. A drastic purge and a light diet are usually sufficient

to clear the eruption in the course of a day or two Local treatment is limited to the application of an antipruritic lead and tar lotion, and the existing eruption can almost always be made to disappear rapidly by the injection of 0·5 ml. of a 1 : 1,000 solution of adrenaline hydrochloride. The antihistamine drugs given three or four times daily usually have a dramatic effect in relieving urticaria and in preventing further attacks. The action of antihistamines is, however, purely symptomatic, and when withheld the eruption recurs unless spontaneous desensitization has taken place. Cases of urticaria which have persisted for weeks or months may be difficult to control as the cause is often never determined. In dealing with such cases a series of simple diets similar to those recommended for certain cases of asthma (see p. 689) may be given to eliminate the possibility of food being the cause, and if necessary a period of starvation may be advised as an aid to dietary investigation While these elimination diets seldom reveal the responsible allergen, the strict regimen involved not infrequently has a beneficial effect Areas of focal sepsis must be sought and dealt with if present. Free elimination must be encouraged by diuretics and an adequate supply of fluids If no cause is discovered, non-specific desensitization may be attempted by a course of peptone injections, or by autohæmotherapy (see p. 691). Ephedrine is often useful, and in a few cases calcium administered by mouth is of service A mixture containing pepsin and hydrochloric acid may be prescribed and will occasionally give relief, but when we are driven back upon such measures therapy has assumed a " hit or miss " aspect. It must be remembered that a certain number of chronic urticarias are really cases of dermographism for which little can be done, although they occasionally respond to alterations in diet even although the skin eruption is not dependent on the ingestion of any particular food Every now and then a case of urticaria is met with which seems to be due definitely to nervous influences, but this type, like that due to heat and cold, is extremely rare

Cutaneous scratch tests with foreign proteins seldom provide any evidence which cannot be obtained by the more direct means of history taking, a complete physical examination and the results of therapy The tests are tedious to carry out, often extremely difficult to interpret, and positive reactions may have no relation to the case Occasionally they demonstrate rapidly the protein to which an intolerance has been developed, but whatever indication is given by the tests it must be verified by therapy, and frequently the results of therapy do not correspond to the results of the test.

Specific desensitization to a protein which is definitely the cause of the eruption is not worth while. It is highly improbable that specific desensitization can be achieved, although over a period of years desensitization may occur naturally and spontaneously

DRUG ERUPTIONS

These, including enema rashes, are by no means uncommon. The majority of them do not itch, so that no treatment is required beyond the discontinuance of the causative drug Morphine and its derivatives, however, can cause a very irritable type of erythematous and urticarial rash which may require the application of a lead and tar or a 1 per cent carbolic lotion to allay the itching. The rashes due to the organic arsenical compounds or to gold run a very

prolonged course, and their treatment has been discussed elsewhere (see p. 282)

BULLOUS ERUPTIONS OF INTERNAL ORIGIN

These include erythema multiforme, dermatitis herpetiformis and the various forms of pemphigus, all of which are of unknown origin. Eruptions due to bromides and iodides, sulphonamides and penicillin may be bullous in character. Very rarely bullæ may develop in urticaria, and varicella and variola are bullous in their initial stages.

In the first group of diseases erythema multiforme is a self-limited disease and the eruption seldom requires more than local palliative measures with antipruritic lotions. In those cases in which the eruption recurs at short and frequent intervals the administration of a sulphonamide preparation in the early stages may reduce the duration of the attack

Some cases of dermatitis herpetiformis are controlled satisfactorily by the internal administration of liquor arsenicalis, some by sulphonamides, and some by avlosulphone. With rare exceptions corticotrophin or cortisone are capable of suppressing the active phase of the disease in every case. The severity of the attack will determine whether one or other of these treatments is instituted, bearing in mind that the disease is chronic in character, subject to remissions and exacerbations of long duration, and that the drugs mentioned may all produce undesirable effects if continued for long periods.

Corticotrophin and cortisone suppress pemphigus in all its forms, and are the only drugs which have so far been found to do so with certainty. They must be used judiciously to sui

manifestations present at

danger to life in some fc

features of others. The

quickly as possible, and the drugs may justifiably be withheld from time to time if the symptoms so warrant.

The local treatment of any bullous eruption consists in snipping the roofs of the bullæ, painting the affected area with ½ per cent. eosin, and applying a protective covering of a paste spread.

HERPES SIMPLEX

At the commencement of an attack, dabbing the irritable tingling area of skin with 5 per cent silver nitrate in spirit of nitrous ether is often sufficient to prevent the further development of the lesions Unfortunately this treatment produces a black stain on the skin, and as the eruption almost always affects an exposed area it may not be feasible to carry it out in every case. After the eruption has developed, a 1 per cent. ammoniated mercury paste is the most

flat glass electrode, may prevent further attacks Vaccination with calf lymph as for smallpox, and also cutaneous vaccination with the fluid obtained from the early vesicles of herpes, seems to stop the recurrences in some instances

HERPES ZOSTER

In the early stages of this condition the injection of pituitrin is said to be useful, both in allaying the pain and in shortening the duration of the eruption. Doses of ½ to 1 ml. can be given once or twice daily for the first two or three days. The affected skin should be powdered with talc and covered with a thick layer of cotton-wool. When crusting has occurred, a 1 per cent ammoniated mercury paste can be substituted for the talc. In herpes zoster affecting the first division of the fifth nerve, great care must be taken of the eye. If lesions develop on the conjunctiva or lids, cold compresses should be used for a day or two and atropine instillations given daily. In ophthalmic zoster involvement of the conjunctiva may not occur until five or six days after the onset of the skin lesions. The after-pain of herpes zoster is treated with simple analgesics of the aspirin type.

LUPUS ERYTHEMATOSUS

The cutaneous manifestations of lupus erythematosus are essentially benign in character, and the disease in this form is of not uncommon occurrence. The lesions are seldom extensive, and only in rare cases do they become widespread and accompanied by symptoms of a severe systemic disturbance. The visceral manifestations which occasionally occur in conjunction with cutaneous lupus erythematosus can be suppressed by corticotrophin and cortisone. Uncomplicated cutaneous lupus erythematosus responds poorly to these agents, but reacts most favourably to mepacrine and chloroquine in ordinary dosage, the latter being much the more suitable drug as it does not cause any discolouration of the skin. A six weeks' course is usually sufficient to clear the eruption, which may or may not leave an atrophic scar.

Cutaneous lupus erythematosus is treated locally with calamine lotion, and small patches may be frozen with CO_2 snow. During an active cutaneous phase exposure to strong sunlight should be avoided, and subjects who have suffered from the disease in the past should take similar precautions.

ALOPECIA

The treatment of alopecia depends on the cause of the condition. That following febrile illnesses or traumatic shock requires no treatment, as the hair grows in normally in due course. Patches of alopecia due to scar formation from whatever cause are permanent and no treatment is of any avail. In alopecia seen in the early stages of syphilis the hair grows in naturally, but regrowth is accelerated by antisyphilitic treatment. The only forms of baldness which definitely benefit from treatment are alopecia areata and alopecia due to deficiency of thyroid secretion.

In alopecia areata counter-irritation either with chemical applications or with ultra-violet light may limit the disease and accelerate regrowth. The following lotion is widely used:

℞	Lactic Acid	24 ml. (6 fl. dr.)
	Castor Oil	12 ml. (3 fl. dr.)
	Industrial Methylated Spirit	to 180 ml. (6 fl. oz.)

Painting the patches [illegible]
useful and may be carri [illegible]
using a mercury-vapour [illegible]
to six weeks, giving an [illegible]
tedious to the patient than a prolonged continuous course lasting for several months. Such short courses can be given at intervals of two months. Attention to the general health and removal of all septic foci should, of course, be considered in addition to the local measures.

PITYRIASIS ROSEA

This condition is self-limiting, and if it does not cause any discomfort it may be left untreated and allowed to disappear spontaneously. There is no doubt, however, that a daily potassium permanganate bath followed by the application of a 2 per cent sulphur and salicylic acid vaseline greatly accelerates the disappearance of the rash. If there is much irritation, a 1 or 2 per cent. tar paste may be used in preference to the salicylic vaseline. Most cases will clear up quickly under the influence of one or two erythema doses of ultra-violet light, but as there is often a certain amount of irritation produced by this treatment, it is questionable if it serves any useful purpose. Pityriasis rosea seems to produce a lasting immunity, and recurrences are practically unknown.

LICHEN PLANUS

Nothing is known regarding the ætiology of lichen planus, although it has [illegible]

[illegible], not
and
[illegible]
large
proportion of cases and also causes the eruption to disappear with moderate rapidity The area of the spine to be treated is that which gives rise to the nerves going to the area of skin affected with the rash.

Internal treatment consists in the administration of calomel in doses of 3 mg. ($\frac{1}{20}$ gr.) three times daily. Arsenic is also useful, and intramuscular injections of Enesol, a preparation containing mercury and salicylarsonate, have been found to give good results. In cases which are very resistant to treatment and in which the irritation is severe, lumbar puncture and the withdrawal of 10 to 20 ml. cerebrospinal fluid may be followed by symptomatic relief. In some cases of lichen planus the eruption disappears promptly under treatment with corticotrophin or cortisone.

PSORIASIS

Success in treatment in psoriasis depends to a large extent on how much time a patient is willing to devote to the cure of the attack and how much inconveni-

ence he is willing to undergo during the treatment Any attack of psoriasis can be cured if a patient will give up his whole time to it, and but for the fact that recurrence is almost invariable, it would be as satisfactory to treat as any other disease. In giving advice to a patient about the treatment of his psoriasis it is necessary to consider whether the amount of eruption present is sufficient to justify putting him to considerable inconvenience and expense, bearing in mind the fact that recurrence will almost always take place. This problem does not arise if a patient insists that he must be made spotless, nor when the eruption is so extensive as to cause a great deal of inconvenience from scaling, cracking and general discomfort. The treatment which will be described applies to psoriasis no matter how scanty or how extensive the eruption, and in addition to this a modified ambulatory treatment will be outlined.

External Treatment.—The treatment should commence with twice daily applications of a 1 per cent tar paste, and the strength of the tar should be increased at intervals of two days up to 5 per cent ; the increase might be graded 1, 3, 5 per cent The tar pastes should be spread on calico Thereafter a 5 per cent chrysarobin paste should be applied twice daily, and it may also be spread on strips of calico or merely rubbed into the skin When it is found that the skin will tolerate chrysarobin, and very few patients suffering from psoriasis seem to be intolerant to it, Dreuw's ointment can be used

This should be rubbed in twice daily and should not be applied spread on strips unless to localized hypertrophic patches If spread on strips and bandaged on, there is a very definite risk of blistering due to the high percentage of salicylic acid present in the preparation Dreuw's ointment causes a blackish-brown discoloration of the skin, and it is superfluous to continue when a thick blackened surface layer has been formed It is then an advantage to interrupt the treatment for two or three days and to use an ichthyol paste ; first, to allow the removal of the black surface skin, and secondly, to give the patient relief from the heat and irritation which almost always accompanies the application of this preparation. The Dreuw's ointment, alternating with the ichthyol paste, is continued until the whole skin surface has become smooth and only staining marks the site of the psoriatic lesions. It is an advantage to give a week or ten days' treatment with crude gasworks tar after the Dreuw's ointment has been discontinued, because if this is done there is less chance of recurrence at an ea- date. Dreuw's ointment and 5 per cent chrysarobin paste can be applied to t scalp provided it is kept shaved, and provided the chrysarobin applications a washed off at night and replaced with tar paste There are two possible dangers ssociated with the application of chrysarobin, one being the production of con-unctivitis, the other the occurrence of an erythematous and later a vesicular dermatitis. Provided the treatment is carefully supervised, the onset of either of these complications need not be considered a serious matter The conjunctivitis can be treated with instillations of castor oil, and the dermatitis will settle very quickly after the chrysarobin is removed with olive oil and a 1 per cent ichthammol paste substituted Another drawback to chrysarobin treatment of which the patient must be warned is staining of bedding, clothing and the bath. A bath need only be given every second or third day when chrysarobin is being used, and care must be taken to clean the bath immediately after use, particularly when the strong applications are being used

If psoriasis is not treated in the fairly drastic manner outlined above, a longer period of treatment will be required. The same sequence of treatment can be

and be given an antiseptic douche. An injection of 2,000,000 units of procaine *penicillin should* be administered if such treatment can be undertaken within 12 hours of coitus.

on each of the subsequent two days

If prophylaxis by early treatment cannot be undertaken within 24 hours it is

under observation. *Instruc-*
it of signs and symptoms of
The patient should be kept
under observation for 3 to 4 months.

GONORRHŒA

The symptoms of this disease are now much less severe than 20 years ago

treatment without exact diagnosis is likely to lead to bad results, and it is obvious that social complications may arise, for example, from false accusations of a wife or husband

The diagnosis is established by the examination of smears and cultures taken from the urethera, cervix and other areas liable to be infected. The use of cultures on an appropriate medium is essential in all cases where the diagnosis may have to be substantiated in a court of law. With good technique cultures will give a much higher number of positive results than the examination of stained smears. The use of Stewart's medium enables swabs to be sent to a distant laboratory, since drying kills the organisms.

ACUTE GONORRHŒA IN THE MALE

of gram negative intracellular diplococci
ould
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not
veral
will
disappear spontaneously If, however, microscopic examination shows many organisms it is advisable to prescribe 1 g of sulphadimidine four times a day along with an abundant fluid intake and this usually proves effective.

Penicillin may be given by mouth instead of by injection, but oral treatment should be used only when injections are impracticable for its effect is less rapid and certain and the patient cannot always be relied upon to take the drug. The best oral preparation is phenoxymethyl penicillin (Penicillin V)

The single dose of procaine penicillin advised (600,000 units) *will suffice to*
discharge or the persistence
-infection. If relapse is the
to a further two doses of
600,000 units of procaine penicillin given at intervals of 48 hours Relapsing

cases require more careful observation and very stringent tests of cure. Penicillin resistant gonorrhœa is almost unknown and is usually due to an enclosed focus of infection. Many cases alleged to be penicillin resistant will be found to be due to infection with other organisms; the nature of the organism and its sensitivity to antibiotics should be determined. Repeated re-infection is occasionally the cause of supposed drug resistance.

The patient is advised to avoid alcoholic drinks for two weeks, and to abstain from sexual intercourse until cure is established. No interference with diet is needed, and as the discharge diminishes rapidly it is seldom necessary to advise special precautions against soiling of clothing and bed linen. The simplest protection is a square of lint pinned inside the vest; clothing or linen which has been soiled by discharge can be sterilised by soaking for some hours in any household antiseptic and then laundered in the usual way. The patient should be encouraged to bathe. The bath may be rendered safe for others by rinsing immediately after use with any weak antiseptic. Care must be taken to avoid the use of towels which may be used by others, especially by young girls.

ACUTE GONORRHŒA IN THE FEMALE

The diagnosis is established by finding gram negative diplococci, usually intracellular, in stained smears taken from the urethra, vagina, cervical canal and the ducts of the Bartholinian glands. At the same time the presence or absence of *Trichomonas vaginalis*, yeasts or other possible causes of vaginitis should be ascertained. Repeated examinations using cultures as well as smears, may be required to establish the diagnosis.

Gonorrhœa in women is readily cured by penicillin, but it is advisable to give procaine penicillin 600,000 units on two successive days. This will cure the great majority, but if complications such as salpingitis or Bartholinian abscess are present more prolonged treatment is needed. If there is coincident infection, e.g. by trichomonas vaginalis, this must also be treated (see p 194).

The same general principles apply to women as to men. Sexual intercourse must be avoided and strenuous sports should not be undertaken during menstruation. A woman may use a sanitary pad as protection against soiling but vaginal tampons are not recommended.

SEROLOGICAL AND BACTERIOLOGICAL TESTS

At the outset the blood of both male and female patients should be tested by the Wassermann reaction or Kahn test for syphilis and the complement fixation test for gonorrhœa (G C F.T.). The tests for syphilis should be repeated at intervals of a month until 3 months have elapsed. This will guard against coincident infection by syphilis, which would be masked but not cured by penicillin treatment. If the G C F.T. is positive at the beginning of treatment the titre should fall rapidly after treatment and be negative within three months. If the titre does not fall or if it rises there are strong grounds for suspecting a focus of persisting infection. In a woman this is most likely to be in the fallopian tubes and in a man the prostate and seminal vesicles are the probable sites.

Tests of the secretions collected from the genito-urinary tract should be made at the end of the first, second and third weeks, and then at the end of two months and three months after treatment. In women the specimens should be obtained immediately after menstruation, or may be taken 24 hours after insertion of a plug soaked in glycerine into the cervical canal and upper vagina. A man should

have prostatic massage performed, and the secretion [illegible]

[illegible] patient can be assured of cure. It is important to be emphatic about cure when this is justified as otherwise many patients have secret fears for years, and this causes much unhappiness.

LOCAL COMPLICATIONS OF GONORRHŒA IN THE MALE

These are now rare in this country; the commonest are prostatitis and epididymo-orchitis.

Acute Prostatitis.—This is associated with severe urinary symptoms and often high fever. The patient should be kept in bed and the pain relieved by appropriate sedatives; some patients will require morphine and atropine. Hot [illegible]

[illegible] if possible The acute symptoms and signs generally subside within 48 hours of treatment with penicillin unless an abscess has formed. Penicillin should be given in large amounts—at least 1,000,000 units per day, and continued for five to seven days. If an abscess has formed it may point into the urethra and when rupture occurs there is a profuse discharge of pus and rapid relief is obtained. *In exceptional cases it may be necessary to drain a prostatic abscess* by perineal incision—this is a major operation of considerable technical difficulty.

Subacute or Chronic Prostatitis.—In the course of gonorrhœa this is not infrequent and may readily be overlooked. Such cases have few symptoms except occasional attacks of frequency of micturition and dysuria On palpation per rectum the prostate is slightly increased in size or tender, and it is often [illegible] seminal vesicles are [illegible]

[illegible] fluid should not contain an excess of polymorphs (i.e. not more than 5 per high power field in a wet specimen) and there should be no organisms present. If fluid is not easily obtained after prostatic massage the urine should be voided into a sterile tube and centrifuged specimens examined. Treatment should be continued until the fluid obtained by prostatic massage is free from pus and organisms

Epididymitis.—This is generally an acute condition ushered in by pain in [illegible] dysuria and fever. Precipitating [illegible] *or occasionally* [illegible] ut is generally relieved by hot kaolin poultices, a supporting bandage and pad, and if necessary analgesic drugs. Rest in bed is generally necessary for a few days. Penicillin *in doses of 600,000 to 1,000,000 units per day should be given for three to five days*; rapid relief of pain and urinary symptoms follows The swelling of the epididymis subsides more slowly and may not be complete for two or three weeks. The majority resolve completely without permanent damage, but a few may have residual fibrosis of the lower pole, and if bilateral epididymitis has occurred sterility may result

Patients who have epididymitis have also infection of the prostate and seminal vesicles and after the acute phase they should be given the treatment advised for subacute or chronic prostatitis

Epididymitis due to organisms other than the gonococcus is not uncommon,

testicular atrophy. The cause is unknown, and no specific treatment is likely to be effective. Tuberculous epididymitis is occasionally mistaken for venereal infection and in those who have lived in tropical countries filarial infection has to be considered In older men a complete genito-urinary investigation should be done to exclude stricture of the urethra and enlarged prostate.

Epididymitis associated with staphylococcal or coliform infections may lead to suppuration The scrotum becomes distended with pus which must be evacuated surgically. In addition active treatment with the antibiotic to which the organism is sensitive must be given.

Balanitis.—Phimosis and superficial erosion of the glans penis and inner surface of the prepuce are often encountered in gonorrhœa Syphilis and chancroid must be excluded Healing is rapid if the gonorrhœa is treated with

field examination of exudate from the abraded area Serological tests for syphilis must be continued for 3 months

Peri-urethral abscess.—This complication of gonorrhœa is now rare and is found mainly in relation to a stricture of the urethra The abscess may point externally, and should be aspirated and penicillin solution (1 ml. containing 100,000 units) injected into the abscess cavity At the same time active treatment of the infected urethra is continued Subsequent dilatation of the urethra is necessary to prevent stricture, but this should be delayed until the inflammation has subsided completely

Conjunctivitis.—Gonococcal infection of the conjunctiva of an adult is rare in Britain, but not uncommon in primitive peoples A very severe inflammation occurs usually causing damage to the cornea and thus impairment of sight. Treatment consists of parenteral administration of penicillin—for example 1,000,000 units at once followed by procaine penicillin, 600,000 units daily for three to five days. This should be supplemented by irrigation of the conjunctival sac with normal saline at blood temperature and the instillation every hour of drops of penicillin solution (10,000 units per ml) for 24 hours After the first day drops of 20 per cent solution of sodium sulphacetamide may be instilled every four hours If treatment is commenced early complete recovery is to be expected.

Skin Infections—Gonorrhœa seldom causes infection of the skin, but occasionally small abscesses occur, especially in the skin of the penis, or a small sinus develops. Infected parameatal glands, or infection of the small Tyson's *glands at the frenum may occur If a collection of pus forms this should be* aspirated or drained and a permanent cure is achieved by destroying the infected duct or sinus by the use of a fine electric cautery.

LOCAL COMPLICATIONS OF GONORRHŒA IN WOMEN

Urethritis.—In women this is seldom troublesome. Infection of the parameatal ducts (Skene's tubules) is best treated by obliteration by electric cautery.

Bartholinian Abscess.—This may be treated by aspiration and injection of penicillin solution. If the abscess has burst leaving a sinus, it is often necessary to drain the abscess more completely by incision, and by packing the cavity.

Vaginitis.—This is generally due to coincident infection by *Trichomonas vaginalis*, yeasts or fungi and the treatment is described on page 180.

Cervical Erosion.—The acute erosion associated with gonococcal infection of the cervix heals rapidly under specific treatment, but chronic erosions, associated with chronic infection with a variety of organisms and damage to the external os, generally require treatment by cauterisation or excision.

Metritis.—This is very frequently associated with salpingitis. The patient should be confined to bed for three to seven days, sedatives and analgesics given to relieve pain and penicillin given in doses of 250,000 units four hourly for three days Relief is usually rapid. Local treatment, especially douching, is

position.

abdom- diagnosis rapeutic rather than surgical and the expectation of complete recovery is reasonable

re cases it may be necessary to give ef may be obtained by hot applications to the lower abdomen. Douching or any form of vaginal treatment is likely to make the patient worse.

The patient is nursed propped up in a semi-recumbent position and times a day and continued until antageous to give sulphonamides the puerperium or after a miscarriage.

If the condition has progressed to pyosalpinx the affected tube and ovary will remain palpable *per vaginam* as a mass in the pelvis, often with widespread adhesions. This can be treated by surgical removal with greater safety and ease after adequate chemotherapy.

In many cases the tubal infection is never acute but presents as a subacute or chronic inflammation, often with extensive adhesions and inflammation in the pelvis, causing recurrent backache, menstrual pain and irregularity, urinary infection and general ill-health. Several examinations may be required before the nature of the infection becomes clear, but a strongly positive G.C.F.T. may indicate the diagnosis.

Treatment consists (*a*) in giving penicillin and sulphonamides for 5 to 10 days—which treatment may be repeated with advantage during the next menstrual period ; (*b*) diathermy directed to the pelvic organs, given daily at

first and later on alternate days for a month ; (c) in a few instances benefit may follow dilatation of the cervix and uterine curettage, but this should not be undertaken till adequate trial has been made of chemotherapy and short wave diathermy, and if extensive damage has occurred it may be advisable to remove the uterus and the useless infected tubes.

Proctitis.—This occurs in both men and women usually as the result of unnatural sexual acts. It may be a sequel to prostatic abscess in a man.

Treatment by injections of 600,000 units of procaine penicillin daily for 3 days may be supplemented by rectal irrigations or the use of suppositories containing proflavine. These are only required when there are extensive areas of infiltration and superficial ulceration, and this is exceptional Proctoscopic examination will indicate how long treatment has to be continued.

METASTATIC COMPLICATIONS OF GONORRHŒA

These are now uncommon and occur mainly in chronic or neglected cases or where inadequate treatment has left an unsuspected focus of infection. Many [illegible]

and limitation of movement of the joint with swelling and redness, and severe fever. If the joint is aspirated or explored surgically it is found to contain a purulent exudate, and often the synovial membrane and the articular surface are eroded. The pus from the joint may contain gonococci, but it is often difficult to find the organism and " negative " reports by the bacteriologist do not contradict the diagnosis

Acute gonococcal arthritis requires vigorous treatment with penicillin, giving 1,000,000 units daily in divided doses for five to ten days, and it is often advantageous to inject penicillin into the joint after aspiration of the pus For this purpose a solution containing 100,000 units per ml is satisfactory. The joint should be partially immobilised, but plaster fixation is seldom required In addition to penicillin it may be necessary to give sulphonamides or tetracycline to control other organisms present in the genital tract. The usual measures for relief of pain are adopted. In gonococcal arthritis it is wise to start passive and active movements as soon as the pain abates, and benefit is obtained from short-wave diathermy. At a later stage massage and exercises will contribute to full recovery of function.

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C[illegible]

of th[illegible]

associated with chronic infection with a variety of organisms and damage to the external os, generally require treatment by cauterisation or excision.

Metritis.—This is very frequently associated with salpingitis. The patient should be confined to bed for three to seven days, sedatives and analgesics given to relieve pain and penicillin given in doses of 250,000 units four hourly for three days. Relief is usually rapid. Local treatment, especially douching, is harmful, and pessaries and tampons are without value. If the vagina is heavily infected it may be treated once daily by swabbing with a dilute antiseptic, using a bivalve speculum, and the patient should be nursed in the semi-recumbent position

Salpingitis.[illegible] om-

[illegible] osis

[illegible] atic

rather than surgical and the expectation of complete recovery is reasonable unless a pyosalpinx has formed

[illegible]

likely to make the patient worse.

The patient is nursed propped up in a semi-recumbent position and penicillin is given in doses of 250,000 units four times a day and continued until the temperature falls to normal. It may be advantageous to give sulphonamides in addition, especially in cases which occur in the puerperium or after a miscarriage.

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Chronic arthritis associated with gonorrhœa is often difficult to diagnose and may simulate closely other types of chronic infective arthritis or rheumatoid arthritis; a strongly positive G.C F.T along with a history suggesting previous

injections of foreign protein may be helpful

progressive dilatation of the stricture by bougies and sounds. This must be done with strict asepsis. In a few instances excision of the stricture is possible. The treatment of the majority of the complications of stricture of the urethra is surgical.

SYPHILIS

In Britain, most European countries and in North America the incidence of early syphilis has fallen dramatically in the last decade. This is attributable in great part to the rapid control of contagion by penicillin, and it is recognised that a much higher proportion of patients now achieve complete cure than with the arsphenamine-bismuth system of treatment. The latter was effective, but many patients ceased treatment when it was still incomplete on account of toxic effects, or simply because the treatment was so protracted. It now seems possible to cure syphilis by a "one-shot" technique, giving at one session a [illegible] ntain an effective penicillin [illegible] iple of such treatment is the [illegible]

DRUG TREATMENT

Penicillin.—It is now generally accepted that penicillin has supplanted *arsenic as the drug of choice in the treatment of syphilis. Penicillin* acts more rapidly and more certainly than the arsenical drugs; the treatment is cheap and safe. The blood level required is believed to be about 0·03 units of penicillin [illegible]

gained, except in very unusual cases, from frequent injections of crystalline penicillin, which will give high blood concentrations; though occasionally, in [illegible]

adult of 10 to 12 stone are :—

Early syphilis (sero negative) . .	6,000,000 units in 10 days.
Early syphilis (sero positive) or within 1 year of infection	12,000,000 units in 20 days.
Late syphilis . .	20,000,000 units in 20 days.

The course may be repeated

The doses given above are average requirements and are empirical. In late syphilis the welfare of the patient and the changes in symptoms and signs should guide treatment rather than a slavish observance of any rigid scheme of dosage or an heroic attempt to reverse positive Wassermann reactions in the blood or cerebrospinal fluid. No authenticated instances of syphilis being resistant to penicillin have been reported, though some cases require higher dosage than others.

Bismuth.—Most American physicians have abandoned the use of bismuth

are given intramuscularly, usually at intervals of five to seven days and are continued for ten to twelve weeks. The precautions necessary prior to each injection are to

the condition of

and the blue li

are unhealthy,

Bismuth is a valuable prelude to treatment with penicillin in late syphilis,

Iodides.—Iodides have some value in assisting the resolution of gummatous lesions and may be prescribed in doses of 1 to 2 g (15 to 30 gr) three times a day in cardiac syphilis, meningo-vascular neurosyphilis and where gummata occur in any organ or tissue. Treatment with iodides should precede for several weeks the administration of penicillin or bismuth in any form of late syphilis

Herxheimer Reactions.—The reaction of Jarisch-Herxheimer may result from the treatment of syphilis by any specific drug which acts quickly. The main features occur within twelve to forty-eight hours of giving an effective dose of the drug and consist of a rise in temperature up to 104° F., a rapid pulse and a general constitutional upset. At the same time the clinical signs of the disease are temporarily aggravated—the skin eruption becomes more intense, the primary lesions larger and more œdematous and the lymph glands more swollen and tender. This reaction is most pronounced in early syphilis, in which it is of little consequence apart from the discomfort which is experienced

reactions (e g. in cardiac

drugs which act slowly-

such therapy the more

safety.

In early syphilis there is no danger from the Herxheimer reaction and the urgent need to control the infection and make the patient non-contagious indicates the immediate use of penicillin in adequate doses. The occurrence of

reaction, continuance of treatment is followed by rapid recovery.

clinical observation. Each case must be considered as an individual problem and treatment by schedule is unwise. Many patients survive for years after severe cardiac and aortic syphilis has been diagnosed and treated.

Syphilis of the peripheral vessels is a comparative rarity and reacts well to the type of treatment advised for gummatous lesions.

SYPHILIS OF THE CENTRAL NERVOUS SYSTEM

General Paralysis of the Insane (G.P.I.).—Dementia paralytica is now usually diagnosed at a relatively early stage and therefore complete or partial recovery is usual. This early stage is often the period of disorders of conduct and [illegible]

uncooperative rather than maniacal or suicidal. Treatment may initially aggravate the symptoms and convert a talkative nuisance into a dangerous maniac. Certification and admission to a mental hospital may be the only way to ensure adequate treatment.

A thorough examination of the nervous system and heart and a lumbar puncture should precede treatment. As a rule it is necessary to give penicillin in full doses without delay of more than a few days, which time will be employed in examination, observation and sedation. The aggravation of symptoms after penicillin may be attended by a febrile reaction and the patient should be confined to bed and given adequate sedation. Procaine penicillin in doses of 600,000 units daily for three weeks is adequate.

Progress and future treatment are governed by clinical observation and tests of the cerebrospinal fluid. As a rule the cell count and protein content of the C.S.F. return to normal within three months, but the positive Wassermann reaction and the paretic gold sol curve remain unchanged for a long time. Some authorities consider it safe to stop treatment when the cell count and protein content of the C.S F. are normal, but in the writer's experience it is wiser to secure reversal to normal of the Wassermann reaction and gold sol test, which usually requires many courses of penicillin and bismuth over a period of one to three years. When clinical recovery and a normal C.S.F. have been attained the patient's future can be regarded with confidence. Nevertheless a few patients are unfortunate and gradual atrophy of the brain, often associated with epilepsy and progressive dementia, occurs even after the apparent arrest of dementia paralytica. The treatment of the epilepsy is symptomatic (see p. 822), but the mental deterioration is not amenable to treatment.

Malarial fever therapy has been almost completely abandoned in favour of penicillin but is still occasionally necessary for those cases which do not respond satisfactorily to penicillin treatment. The inoculation of a strain of benign tertian malaria is usually employed, but higher and more accurately sustained temperatures over more prolonged periods can be achieved by treatment in a special fever cabinet, and this artificial fever is less dangerous than malaria. Fever induced by vaccines seldom benefits G.P.I

The contra-indications to fever treatment are an age over 55, maniacal excitement, nephritis, hypertension, severe cardiovascular disease, gross obesity and pregnancy. Preliminary tests should therefore include a radiograph of the heart and aorta, an electrocardiographic examination, tests of the urine and an estimation of the non-protein nitrogen of the blood.

Treatment by fever cabinet, though more efficient, is only available at a very few centres. Temperatures of 105° F. to 106° F. should be maintained for four to six hours and the sessions repeated on 8 to 12 occasions The patient should be given 1,000,000 units of penicillin just before entering the cabinet as there is some evidence that penicillin penetrates the brain more readily during fever.

If it is desired to give malarial therapy a supply of blood containing the parasites of a known safe benign tertian strain can be obtained from Horton Mental Hospital, Epsom. The blood (5 to 10 ml) is inoculated intramuscularly. The incubation period is about ten days but may vary from five to twenty-one days Malarial parasites appear in the blood soon after the onset of fever. No isolation of the malarial patient is necessary in Britain, but the most careful nursing is required as the treatment is not without risk. Death may occur from hyper-pyrexia, circulatory failure or uræmia After 8 major pyrexial attacks the malaria may be stopped rapidly and permanently by the usual treatment (see p 198).

The prognosis depends more on early treatment than on the severity of the symptoms. Maniacal or very depressed patients may recover completely, but if gross mental deterioration has occurred partial recovery and arrested progress of the disease is the best that can be expected. But even such advanced cases are happier and more easily managed after treatment, and with mild euphoria and some amnesia they may appear very happy if unproductive citizens

Tabes dorsalis.—This condition responds moderately well to specific treatment provided this is started at an early stage, and some improvement may be expected in all but the most advanced cases.

The general treatment follows the lines advocated above, namely prolonged [illegible] recovery. Fever therapy usually makes tabetics worse, but may be tried after other remedies have failed, in cases of severe tabetic pains and crises Fever may also be indicated in rapidly progressing optic atrophy. It is most convenient to describe the treatment of tabes dorsalis under the headings of the commonest symptoms of the disease

Visual failure due to optic atrophy is often advanced before being diagnosed and the response to treatment is very disappointing, but in about 30 per cent of cases its progress may be arrested A very short period of treatment with iodides and bismuth—e g ten days—should be followed by penicillin, and this should be continued [illegible] after an interval of four weeks a second course, [illegible] rogress should be assessed by [illegible] In cases where deterioration [illegible] courses of penicillin, fever therapy is indicated. The patient's health should be improved as much as possible by attention to diet, rest, etc , and it is often necessary to change his occupation. If there is severe loss of vision he should be registered as a "blind person" and training commenced under the auspices of the various societies who assist the blind Quite often such blind persons acquire a high degree of skill and remain happy and useful citizens (see p. 843)

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prolonged treatment with daily doses of 2 g. may be effective. A further course of treatment is necessary in about 10 per cent. of cases. Dosage with one or other of the tetracyclines should be 1 g. a day in divided doses for five to ten days. Chloramphenicol is less effective than the other antibiotics mentioned Prolonged supervision is advisable to detect relapse.

LYMPHOGRANULOMA VENEREUM

This virus infection is resistant to sulphonamides and penicillin, though these drugs may improve superimposed infection with other organisms The tetracyclines in divided doses of 2 g. per day for ten days provide the most effective treatment. It is important to test for coincident syphilis. Surgical treatment for ano-rectal stricture may prove necessary, but the bubo should not be incised.

VENEREAL WARTS

Warts on the genital area are a local infection without systemic effects and [illegible]

infiltrate the wart-bearing area with 1 per cent. procaine and then to destroy the pedicle of the warts with the electric cautery. The cauterised area is kept dry by dusting with talc powder. If the warts have extensively invaded the urethra, [illegible]

by lanoline, and a 20 per cent suspension of the resin in liquid paraffin should then be applied by means of a dressed probe or matchstick. This is allowed to dry for ten minutes and the area should then be covered with dry gauze, the podophyllin being washed off after four hours. A rather less effective but more convenient preparation is a 20 per cent. extract of podophyllin resin in spirit. Considerable irritation of skin and mucous membrane may result from podophyllin applications

TRICHOMONAS VAGINALIS INFESTATIONS

Trichomonas Vaginalis Infestations.—This parasite is a common cause of vaginitis and possibly other inflammations of the female genital tract; in addition it may cause urethritis and balanitis and possibly prostatitis in the male. In many men the parasite may cause no symptoms but exists in the genital tract for a short time after coitus The man in this way may be a carrier and may be responsible for the repeated reinfection of his consort. But there is some evidence [illegible] *Trichomonas vaginalis* disappears spontaneously

[illegible] use of acetarsol vaginal [illegible] vagina at night. The treatment is continued for several weeks and should be repeated throughout the next menstrual period and for two days afterwards. In addition to the suppositories the woman should bathe the vulva and perineum frequently and after drying should apply a dusting powder freely. In very acute cases it may be preferable to douche the vagina with warm saline and then apply acetarsole compound in powder form with the aid of a speculum.

[illegible] in the Male.—*Trichomonas vaginalis* infection [illegible]

best treatment is to irrigate it twice [illegible]

[illegible] days and to administer potassium citrate in sufficient [illegible]

FUNGOUS INFECTIONS

In the male balanitis and urethritis due to fungous infections are usually associated with glycosuria (see p. 289) or with fungous infection of the skin of [illegible] area (see p. 156).

[illegible] in pregnancy and is [illegible]ated [illegible]ated through a speculum with 2 per cent [illegible] be repeated on several occasions at intervals of a few days. The antibiotic Nystatin is effective when applied locally in pessaries

PARASITIC INFECTIONS

Scabies.—*In some cases scabies may be acquired venereally, and starting on the ano-genital region may be confined for a time to the genitals or buttocks. The treatment is described on p 157*

Pediculosis Pubis (" Crabs ").—*This is often a venereal infestation and is frequently overlooked Its treatment is discussed on p 159*

R. LEES

COMMON TROPICAL DISEASES AND HELMINTHIC INFECTIONS

INTRODUCTION

THE SELECTION of the tropical diseases, the treatment of which is discussed in this section, was made primarily to meet the requirements of students and practitioners in Great Britain. In the course of their practice they are likely to meet some of these diseases, especially with present-day greatly increased speed of travel. Some tropical diseases have been omitted, not because they are unimportant but because it is unlikely that they will be seen in this country. Other diseases usually included in textbooks on tropical diseases are dealt with in other sections of this book.

Many of the tropical diseases tend to *run a very acute and fulminating* course and may end fatally if not diagnosed early and given proper treatment. It is therefore most important that medical men in non-tropical countries should be able to recognize these diseases and know how to treat them.

Malaria and amœbic dysentery are the two tropical diseases most commonly seen in this country, hence their treatment has been dealt with in more detail.

The practitioner will be asked by patients proposing to go to the tropics what precautions can be taken to prevent infection To help him, a brief account of methods of personal protection has been included with each disease.

MALARIA

Cycle of Development of the Plasmodium.—To have a proper understanding of the therapeutics of malaria, it is necessary to recollect certain points in connection with the life cycle of the malaria parasites. The sporozoites injected into man by the female of the genus *Anopheles* disappear from the circulation within two hours and enter the liver cells, where a pre-erythrocytic cycle of development takes place. In the case of *P. falciparum* infection, after six days (eight days in *P. vivax*) merozoites are liberated from the liver and enter the erythrocytes. After *P. vivax* parasitæmia is established, an exo-erythrocytic stage of the parasite usually persists in the liver cells. This is very important from the therapeutic point of view: these exo-erythrocytic parasites are unaffected by ordinary antimalarial drugs and their persistence accounts for the relapses so characteristic of *P. vivax* and *P. malariæ* infections. No similar phase has, however, been found in *P. falciparum* malaria, and this explains the absence of relapses in *P falciparum* malaria after adequate treatment. In all forms of malaria, male and female gametocytes appear during the erythrocytic phase and these—when taken up by the mosquito—produce the sporozoites which transmit the disease to other susceptible people. So far no drug is known which will destroy these sporozoites. The clinical manifestations of malaria in man are associated only with the asexual life cycle of the parasite. The existence of gametocytes is *compatible with normal health in the host.*

Recent Developments in Antimalarial Drugs.—From the seventeenth

treatment of malaria and for suppression of the disease in those exposed to the risk of infection. When taken over a prolonged period, mepacrine causes a yellow discoloration of the skin. Toxic effects, nausea, vomiting and diarrhœa occasionally result, and very exceptionally, after prolonged use as a suppressant, eczematoid or lichenoid skin lesions develop. A toxic psychosis with mental excitement or confusion has also occurred, especially with large dosage.

The 4-aminoquinoline group of antimalarials, chloroquine (Nivaquine, Avloclor) and amodiaquine (Camoquin), came into general use about 1944, and have proved to be very valuable antimalarials both in treatment and for suppression. They do not stain the skin and seldom produce any marked toxic effects. Headache, pruritus and blurring of vision may occur with therapeutic doses but disappear after stopping the drug. The effect on vision makes chloroquine unsuitable for aeroplane pilots.

All these antimalarials have a marked action against the erythrocytic phase of all forms of malaria parasites, but they do not affect the exo-erythrocytic phase of *P. vivax* and *P. malariæ* responsible for the relapses in these forms of malaria. In 1945, as a result of studies on the anti-malarial action of the biguanides, proguanil (Paludrine) was shown to have

less. The absence of taste is an advantage for children. On the other hand, fatalities have occurred when children have got hold of and consumed large numbers of pyrimethamine tablets. Both proguanil and pyrimethamine are too slow-acting for use alone in the treatment of an acute attack of malaria.

Pamaquin (Plasmoquine), was introduced in 1926 and proved to have a powerful action against the sexual forms of the plasmodium. It was also

and occasionally a serious acute intravascular hæmolysis similar to that found in blackwater fever. Its action against the sexual forms was therefore not of practical value in reducing infectivity in mosquitoes. Recently less toxic and more effective compounds of this group have been evolved. Primaquine is the best of these, but even with primaquine the patient must be under close medical supervision whilst taking the drug.

General Management of a Patient.—The patient is nursed in bed and given treatment to relieve any troublesome symptoms. During the cold stage extra blankets and heat will be required, but with the onset of the hot stage bed-clothing has to be reduced, and when the temperature ...
cold sponging is needed. The patie...
freely, and aspirin may be given for tl...
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effects. Headache, pruritus and blurring of vision may occur with therapeutic doses but disappear after stopping the drug. The effect on vision makes chloroquine unsuitable for aeroplane pilots.

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Radical Cure of Relapsing Malaria.—All forms of malaria respond to antimalarial treatment, but recurrences are liable to occur except in *P falciparum* infections. These relapses are due to the persistent exo-erythrocytic phase and may recur at intervals over a period of many months The disease can, however, be eradicated by the administration of one of the 8-aminoquinoline compounds Primaquine is the least toxic and most effective member of this group Each tablet contains 7 5 mg base, and the usual dose for an adult is 2 to 3 tablets daily for up to fourteen days This treatment is combined with the ordinary therapeutic course of chloroquine or quinine, but not mepacrine Such a course gives a radical cure rate of around 95 per cent in patients suffering from relapsing malaria. While taking primaquine, the patient must be under close medical supervision and the drug discontinued at once should signs of toxicity occur. Coloured races, being more susceptible, should be given smaller dosage.

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Treatment of Complicated "P. falciparum" Infection.—Immediate antimalarial treatment is required in all patients with a *P. falciparum* malaria. When the attack is complicated by hyperpyrexia, vomiting, collapse or coma, ... becomes a matter of great urgency. In

and where necessary this dose can be repeated in four to six hours. Not more than 1.8 g. (30 gr.) should be administered intravenously in the twenty-four hours, and the oral route is used as soon as possible. Such patients are often so severely dehydrated that they require saline infusions. The quinine solution can then with advantage be added to the infusion fluid.

A soluble preparation of chloroquine suitable for intravenous use is now available in ampoules which contain 0.2 g. of the base in 5 ml. Excellent ... adult, 0.2 to ... is dose as ... dy-weight.

This treatment does not, like quinine, carry the risk of intravascular hæmolysis

(blackwater fever). This chloroquine solution is also convenient for intramuscular administration Apart from the anæmia associated with blackwater fever, a grave degree of anæmia may occur with a heavy *P. falciparum* infection. This may necessitate a blood transfusion as a life-saving measure. Where coma persists despite adequate specific treatment, improvement may result from lumbar puncture and the removal of cerebrospinal fluid

Radical Cure of Relapsing Malaria.—All forms of malaria respond to antimalarial treatment, but recurrences are liable to occur except in *P. falciparum* infections These relapses are due to the persistent exo-erythrocytic phase and may recur at intervals over a period of many months The disease can, however, be eradicated by the administration of one of the 8-aminoquinoline compounds Primaquine is the least toxic and most effective member of this group. Each tablet contains 7 5 mg base, and the usual dose for an adult is 2 to 3 tablets daily for up to fourteen days. This treatment is combined with the ordinary therapeutic course of chloroquine or quinine, but not mepacrine Such a [illegible]

dosage.

The table on p 200 gives suitable curative and prophylactic courses of treatment for the various antimalarial drugs in different age-groups

Blackwater Fever.—This serious and urgent complication of chronic *P. falciparum* infection is much less frequent since the introduction of the newer antimalarial suppressive drugs It may, however, still be seen even in [illegible]

is most frequently provoked by the administration of quinine It is therefore important when treating a patient suffering from chronic *P falciparum* malaria to keep this in mind, and where possible to prescribe chloroquine instead of quinine.

So far we have no real understanding of the cause of the hæmolysis; but cortisone, which has been shown to be of use in certain haemolytic diseases, has recently been employed in the treatment of blackwater fever and has apparently prevented further haemolysis (see cortisone in haemolytic conditions, p 427) Apart from control of the haemolysis much can be done to improve the patient's prospects of recovery, absolute rest is essential even in [illegible]

[illegible] renal [illegible]

to loss of red cell mass, and transfusion must, therefore, be started early, blood carefully matched for compatibility. This is a life-saving

Causal Prophylaxis and Suppression.—The sporozoites introduced by the female *Anopheles* are not susceptible to any known antimalarial drug Clinical attacks of malaria can, however, be prevented by drugs which attack the plasmodium either in its pre-erythrocytic forms (causal prophylaxis) or after it has entered the

protection against clinical attacks of malaria. Very occasionally a strain of plasmodium resistant to these two drugs is encountered; this is considered to be caused by irregularity in the use of the suppressive treatment. These proguanil- and pyrimethamine-resistant strains are, however, susceptible to the other antimalarial drugs The adult protective dose of proguanil is 1 tablet (87 mg. base) daily, starting on the day prior to entering the malarious area. For pyrimethamine the adult dose is one tablet (25 mg base) once a week, also to be started just before entry. The suggested dosage for the younger age-groups is shown in the Table on page 200. Both these drugs are non-toxic; they also inhibit the development of the sexual cycle of the plasmodium in the mosquito. Chloroquine and amodiaquine are reliable sup

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must be taken with the utmost regularity in the required dosage Severe attacks of *P. falciparum* malaria have occurred after leaving the malarious area when the suppressive drug has been discontinued. To prevent this it is important that the suppressive dose should be continued for three weeks after departure. This will ensure destruction of all the *P. falciparum* parasites.

Personal Protection in Malarious Areas.—A very considerable degree of protection against the bites of *Anopheles* mosquitoes can be obtained by the use of long trousers, shirts with long sleeves, mosquito boots after dusk, and sleeping under mosquito nets. Spraying the inside walls of houses with a residual insecticide, or the use of an ærosol " bomb ", will reduce the number of mosquitoes (see Insecticides, p. 232). Nevertheless, the protection afforded by antimalarial drugs is so great that they should always be used in addition. In areas where *P vivax* and *P. malariæ* malaria occurs, only protection from mosquitoes prevents relapses after giving up the suppressive drug on leaving the area

AFRICAN TRYPANOSOMIASIS

It is essential that the diagnosis of trypanosomiasis should be made as early as possible, since delay may lead to invasion of the cerebrospinal system when treatment is much less likely to be successful.

Specific Treatment.—

African trypanosomiasis

acute infections, but they

sequently are of little use in the later phases of the infection. Tryparsamide is able to penetrate this barrier and is therefore used during this stage, especially when the cerebrospinal system has been invaded by the trypanosomes. It is

usually combined with suramin or pentamidine. Arsenic resistance is likely to develop in strains of trypanosomes treated with tryparsamide. The melarsen drugs should be used in such cases.

Suramin (Antrypol, Bayer 205, Germanin, Fourneau 309) is a complex organic urea compound which can be given either intravenously or intramuscularly but not subcutaneously, since it is painful and may cause destruction of the skin. It is advisable to make the first dose a small one, 0·2 g., to test for sensitivity, after which the dose can be increased to 1 g. dissolved in 10 ml. of distilled water, and given at intervals of three or four days up to a total of from 5 to 10 g. Children tolerate the drug well, a safe single dose for a child under three years of age is 0·25 g.; from three to ten years 0·5 g., and over ten years 1 g. doses can be given. Early infections with *T. gambiense* respond well to suramin. Toxic effects, skin eruptions or nausea and vomiting may occur soon after the course is started. During treatment the urine should be examined before each injection for the presence of albumin; if this is encountered, the course need not be stopped but may require modification. The drug is very slowly excreted and so can be used as a prophylactic against infection.

Pentamidine diisethionate, an aromatic diamidine compound, has marked trypanocidal properties. It produces no serious toxic effects even when given in combination with tryparsamide. The dose is 4 mg. per kg. body-weight; in adults an initial dose of 25 mg is followed by 0·2 g. given intramuscularly or intravenously daily for twelve to fifteen days. When the intravenous route is employed, a fall of blood pressure is likely to occur; the injection should therefore be given slowly with the patient recumbent. To counteract the hypotension, the injection may be preceded by 0·5 ml. of 1 : 1,000 adrenaline hypodermically. The course of treatment may safely be repeated after an interval of two weeks. Intramuscular injections are painful.

Tryparsamide (Sodium-N-phenylglycineamide-*p*-arsonic acid employed when the central nervous system has been invaded. It is venously in doses of 2 to 3 g. in 10 ml. of pyrogen-free distilled wat seven day intervals for five to ten injections. Children do not tolerate well; the dose is $\frac{\text{age in years}}{20}$ of the adult dose. Serious toxic atrophy or exfoliative dermatitis, may occur. The acute onset of bl after one injection is very rare. Usually the ocular symptoms are of gr onset, preceded by photophobia, lachrymation and ocular pain. Later, dimne of vision and flashes of light may be present along with contraction of the visual fields; eye changes should be sought for before each injection so that treatment can be stopped if necessary and dimercaprol (BAL) treatment started. The course of tryparsamide may be repeated after an interval of a month. When the central nervous system has been invaded, cure of the disease cannot be accepted until the cerebrospinal fluid has remained normal for six months.

Combined pentamidine-tryparsamide treatment is employed to obtain the synergic action of these drugs. A suitable combined course is pentamidine 0·2 g. intramuscularly daily for seven days concurrently with tryparsamide 2 g. intravenously, at five-day intervals for 8 to 10 doses; the first dose of tryparsamide is given at the same time as the first dose of pentamidine. In *T. rhodesiense* infection, if the diagnosis has been delayed longer than four weeks, invasion of the central nervous system will have occurred, when eradication is very difficult. Some recently introduced arsenicals have, however,

Causal Prophylaxis and Suppression.—The sporozoites introduced by the female *Anopheles* are not susceptible to any known antimalarial drug. Clinical attacks of malaria can, however, be prevented by drugs which attack the plasmodium either in its pre-erythrocytic forms (causal prophylaxis) or after it has entered the erythrocytes (suppression). A small dose of proguanil or pyrimethamine will destroy the pre-erythrocytic forms of *P. falciparum*. Since they also act on the asexual erythocytic forms of all species of human malaria parasites they afford reliable protection against clinical attacks of malaria. Very occasionally a strain of plasmodium resistant to these two drugs is encountered; this is considered to be caused by irregularity in the use of the suppressive treatment These proguanil- and pyrimethamine-resistant strains are, however, susceptible to the other antimalarial drugs. The adult protective dose of proguanil is 1 tablet (87 mg. base) daily, starting on the day prior to entering the malarious area. For pyrimethamine the adult dose is one tablet (25 mg. base) once a week, also to be started just before entry. The suggested dosage for the younger age-groups is shown in the Table on page 200. Both these drugs are non-toxic; they also inhibit the development of the sexual cycle of the plasmodium in the mosquito. Chloroquine and amodiaquine are reliable suppressants without the disadvantages of mepacrine. Drug resistance to this [illegible] quine is 2 tablets [illegible] week, or half this [illegible] unes the suppressive dose of all these drugs can be reduced. Suppressive treatment to be effective must be taken with the utmost regularity in the required dosage. Severe attacks [illegible]

will ensure destruction of all the *P. falciparum* parasites.

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AFRICAN TRYPANOSOMIASIS

It is essential that the diagnosis of trypanosomiasis should be made as early as possible, since delay may lead to invasion of the cerebrospinal system when treatment is much less likely to be successful.

Specific Treatment.—Three drugs are commonly used in the treatment of African trypanosomiasis Suramin and pentamidine give good results in early acute infections, but they cannot pass the " blood-brain barrier " and consequently are of little use in the later phases of the infection. Tryparsamide is able to penetrate this barrier and is therefore used during this stage, especially when the cerebrospinal system has been invaded by the trypanosomes It is

usually combined with suramin or pentamidine. Arsenic resistance is likely to develop in strains of trypanosomes treated with tryparsamide. The melarsen drugs should be used in such cases.

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damage and anuria. It is vitally important that treatment should be started at the earliest possible moment before kidney damage has occurred. The patient should be kept quiet and may be allowed small quantities of fluid by mouth to make him more comfortable. *Purgatives are usually harmful* and little has been achieved by the administration of drugs in an attempt to destroy the toxins in the intestine. In a cholera epidemic the majority of the cases are

intravenously at a rapid rate, up to 100 ml per minute at first. This will soon relieve the painful muscular cramps, but to correct the dehydration as much as 5 to 10 litres of fluid may be required.

For an anæmic patient, estimation of fluid volume requirements on whole-blood specific gravity
more accurate to esti
Fever, p. 199). This,
is being separated. Repeated specific gravity determinations may be carried out at intervals till diarrhœa has ceased, but a knowledge of the quantity of fluid lost and the clinical condition of the patient provides much the most useful guide to the degree of dehydration and the amount of fluid required to correct it. Additional fluids are given as required to replace that lost by the continued diarrhœa and vomiting

Intravenous Infusions.—Fluid must be given rapidly by the intravenous route. The ordinary peripheral veins are tightly constricted and difficult to enter, and must therefore be exposed, or one of the larger veins, such as the 18 B.W.G., is warmed above on stage of the hroughout the illness and the urinary output measured.

As both salt and water are being lost in the evacuations, the replacement should be principally by isotonic (0 9 per cent) saline. A considerable loss of alkalies, however, occurs from the bowel and steps should therefore be taken to combat the resultant tendency to a
half the fluid volume required for in
bonate and half by isotonic saline.
bicarbonate solution should be given in the initial rehydration. To prevent
fluid required to maintain

water is autoclaved, cooled below 40

added. It is then passed through a sterile filter paper to keep back gross insoluble particles, Resuscitation with normal saline and sodium bicarbonate solution should be continued till the fluid loss has been replaced Once a free flow of urine is established, intravenous 5 per cent. glucose is needed only if the patient is unable to take sufficient fluid by mouth As much fluid as possible should be taken by mouth as soon as it can be retained.

No attempt should be made to replace the potassium loss until the kidneys have started to function freely Then potassium citrate, 2 to 4 g., should be given three times a day by mouth Intravenous potassium chloride can be given safely only when facilities are available for blood potassium estimation. A careful watch is kept on the quantity of urine passed For a 60-kg. adult 800 to 1,000 ml. of urine should be passed in the twenty-four hours, and if it falls below 500 ml., potassium administration should be stopped If anuria occurs, the prognosis is very grave Attempts may be made to relieve this by heat to the loins and other methods, but these are not often successful and intragastric drip feeds, as recommended for the relief of anuria in blackwater fever, should be instituted (see p. 201) Favourable results from the use of corticotrophin and cortisone have been reported in a limited number of cases of cholera.

General Management.—During the acute phase of cholera, everything [illegible] other bland foods may be added as desired by the patient Convalescence is usually rapid and satisfactory once the acute stage has been survived without [illegible]

[illegible] in two doses, 0.5 and 1 ml., representing 4,000 and 8,000 million organisms respectively, at seven to ten days' interval. Immune bodies can be detected in the blood by the fourth day and may remain up to six months, but valid statistical evidence confirming the value of cholera vaccination has not yet been presented. All drinking-water and milk should be boiled All food should be protected from flies, and uncooked vegetables as well as raw and unripe fruit should be avoided

AMŒBIASIS

INTESTINAL AMŒBIASIS

Specific Treatment.—Drugs commonly used are emetine, chiniofon, Diodoquin, carbarsone, acetarsol, chloroquine and various antibiotics. Where there are symptoms of active amœbic disease, treatment must be started without delay, but where amœbic cysts only are discovered in a person who has no clinical symptoms of the disease, then the call for treatment is not so clear. If cysts are found in a person who, in the course of his work, is likely to contaminate food, then treatment should be given. Otherwise each case must be decided separately, the possibility of the occurrence of a liver abscess being balanced

amœbic hepatitis. Its use is specially indicated in a patient with myocardial damage where the use of emetine has an additional risk. A combination of these two drugs may be employed in cases which have proved resistant to treatment with either drug when given separately.

When the response to treatment is unsatisfactory, the temperature not settling to normal and enlargement and tenderness of the liver persisting, the presence of an abscess requiring aspiration must be suspected. Even though the diagnosis of abscess is made at the onset, it is important to give emetine for several days before aspiration which should be done in the operating theatre under strict aseptic precautions For exploration of the liver, a large calibre

but a local anæsthetic down to the capsule of the liver is usually sufficient. The needle is inserted, where necessary, down to a depth of three and three-quarter inches, suction being maintained all the time. If the abscess is not found at the first exploration, the point of the needle should be withdrawn to the interspace and re-inserted into the liver in a different direction. Three explorations through one skin puncture may thus be made. Where necessary, further

by attaching the needle to a Potain's aspirator. The size of the abscess may vary from a few millilitres up to three litres. As much as possible should be aspirated from the cavity and the procedure should be repeated without delay if the response to the initial withdrawal of fluid and drug treatment is not fully satisfactory. Open drainage is no longer practised except when secondary infection is present. Little is to be gained by the introduction of emetine or chloroquine into the cavity, but this is still recommended by some. A specimen of the fluid withdrawn should be examined in the laboratory to exclude a secondary infection.

Where bacterial infection is present, sensitivity tests should be carried out on the infecting organism, but immediate clinical trial of antibiotics should not be omitted. Even with the aid of antibiotics, however, open drainage will be needed in most cases with an established secondary infection. In such cases the prognosis is much less favourable. Occasionally more than one abscess

drain the remaining abscess Following resolution of the liver abscess, it is advisable to give a course of treatment for intestinal amœbiasis even though amœbæ are not found in the stools, otherwise re-infection of the liver from the

satisfactory response to treatment, amœbic

course of treatment will be required.

r observation for at least a year.

usually due to direct extension of the

he abscess may rupture into the base

of the right lung or into the pleural cavity. With involvement of the lung

parenchyma, a bronchial fistula may occur allowing the contents of the cavity to to coughed up In such circumstances recovery often takes place with the administration of emetine and with postural drainage. If unsuccessful, surgical aid will be required. Where the pleural cavity has been invaded with material from a sterile abscess, conservative treatment with emetine and aspiration of the pleura and liver should be tried When, however, infection is present, open drainage must be employed Involvement of the peritoneal and pericardial cavities may very occasionally occur If the abscess is sterile, removal of the irritating material by simple aspiration and emetine treatment may be all that is required, but the prognosis must always be very guarded.

LAMBLIASIS

Giardia lamblia is a flagellate whose presence in the intestine is frequently associated with diarrhœa and abdominal symptoms. Outbreaks of diarrhœa associated with heavy infections of giardia are by no means uncommon in Children's Public Day Nurseries in this country.

Mepacrine, in doses of 0·1 g three times a day after food, for up to ten consecutive days in an adult, and a proportionately smaller dose for children, may get rid of this infection, but even repeated treatments fail on occasions The infection tends to lessen when the stools become more solid, and this may follow the administration of bismuth salicylate given in 3 g doses three times a day.

THE MALABSORPTION SYNDROME

It is essential before starting treatment of a patient with a malabsorption syndrome to be sure that the failure in intestinal absorption is not caused by some mechanical defect, such as a short-circuit in the bowel or blockage of the lacteals in the mesentery by a disease process such as tuberculosis or neoplastic growth A further cause may be a defect in the pancreatic secretions preventing the proper preparation of the food for absorption When these causes have been excluded, the presence of an excess of split fats in the fæces in a patient who has [illegible]

anæmia In such a case, unless the stool is examined and analysed, the true cause of the anæmia may be entirely overlooked

IDIOPATHIC STEATORRHŒA

(Adult Cœliac Disease, Non-tropical Sprue)

The clinical picture of this disease is very similar to that found in tropical [illegible]

being abandoned.

TROPICAL SPRUE

The cause of sprue still remains uncertain. Some consider that rancid unsaturated fatty acids, by irritating the small intestine, cause an increased production of mucus which interferes with the normal absorption of food. More recently the importance of the bacterial flora has again been emphasised and good results, in early cases, have been reported following treatment over a prolonged period with a series of different antibiotics, each being given for three or four days.

Impaired absorption of fats and carbohydrates usually leads to a fatty diarrhœa and abdominal distension; such symptoms can be relieved by limitation of these articles in the diet during the early stages of treatment. Absorption defects of other essential constituents in the food will sooner or later lead to a macrocytic anæmia, glossitis and ulcers in the mouth. Tetany, due to hypocalcæmia, is also present in a proportion of cases, and hypoprothrombinæmia, from poor absorption of fat-soluble vitamin K, sometimes predisposes to hæmorrhages. Where a macrocytic anæmia is the chief presenting feature, treatment for pernicious anæmia may be given in error, and it is only the poor clinical response that leads to further investigation and eventually to a correct diagnosis When the patient is severely ill, rest in [illegible] during the initial stages of treatment.

[illegible]

intramuscular injection, say *in a dosage of 15 mg. daily for a week*, but thereafter it is sufficient to give 20 mg. daily by mouth. According to the response, this may be reduced later to 10 mg. daily. However, some patients have to continue *taking this dosage indefinitely*. Since in a certain proportion of cases of tropical sprue there is malabsorption of vitamin B_{12}, it is perhaps advisable to give 100 mg. of cyanocobalamin monthly by injection in addition to the folic acid [illegible]

extract might be given in addition, in a dosage of 4 ml. twice weekly, for a trial period. It is reasonable to assume that there is in some instances malabsorption of various members of the vitamin B complex from dietary sources, and it is *advisable to give* a multivitamin preparation to combat the ensuing deficiencies. It is usually sufficient to give this by mouth, since it is believed that much of the oral dose can be absorbed. Accordingly a capsule containing approximately *the following*: *thiamine* 10 mg , riboflavin 5 mg., nicotinamide 50 mg., should be given twice daily. Glossitis, which may be troublesome, usually clears rapidly with the addition of these essential factors.

[illegible]

Minced lean steak given 60 g. (2 oz.) at a time and gradually increased to [illegible] of 0 67 to 0 90 kg. (1½ to 2 lb.) daily, is usually well tolerated; chicken, liver and fish (not fried) are useful substitutes. Equally satisfactory results are

obtained in the early stages of treatment with a skimmed milk diet, given at first in small frequent feeds of about 240 ml. (8 fl oz.) every two hours during the daytime Sprulac, a defatted dried milk, if available, is a very convenient substitute for fresh milk. Lightly boiled or poached eggs should be added to the diet as improvement occurs [illegible] as stale bread or toast without bu[illegible] well tolerated. Fresh fruit, esp[illegible] allowed, also tomato juice The fats and carbohydrates in the diet are gradually increased, keeping a careful watch on the stools and on the abdomen for flatulent distension A gluten-free diet gives disappointing results in tropical sprue

A sprue patient requires very careful handling from a psychological point of view, and everything must be done to encourage him to expect a complete recovery from his illness Without the full co-operation of the patient, recovery is likely to be delayed. Each patient must be treated as an individual problem; in one the diet may be stepped up very quickly and in another more slowly if diarrhœa and flatulence are to be avoided.

Treatment of Complications.—If tetany develops, calcium gluconate (10 ml of a 10 per cent. solution) should be given at once *slowly* intravenously. Simultaneously, large doses of calcium lactate can be given by mouth (teaspoonful doses every two hours) and the effect can be reinforced by means of vitamin D as calciferol (p 369). Bleeding may occur as a result of hypoprothrombinæmia from poor absorption of vitamin K. When this is severe, a fresh blood transfusion is of great value. Subsequently, 20 mg of menaphthone (which can replace vitamin K_1 and K_2) should be given daily by injection until normal prothrombin values are obtained.

Maintenance Treatment.—The majority of sprue patients, especially if the disease is diagnosed and treated early, make a perfect recovery and are restored to normal health. They may even be allowed to return to the tropics after they have remained well on normal diet for a year Some patients, however, respond less satisfactorily to treatment and may have to limit their intake of fats and carbohydrates indefinitely. This small group often requires a small maintenance dose of folic acid and cyanocobalamin to keep the blood normal.

LEPROSY

Patients discharging leprosy bacilli or from whom bacilli can be obtained by skin slit or scraping of the nasal mucosa should be segregated until controlled by treatment. Those with closed infections, the neural or tuberculoid cases, need not be segregated. All should be treated, and in Britain the Medical Officer of Health must be notified.

Specific Treatment.—The introduction of the sulphone series of drugs has been a great advance in the treatment of leprosy. Dapsone (DDS) diamino-diphenyl-sulphone and derivatives such as solapsone (Sulphetrone) are now available for the treatment of all forms of leprosy. There are, however, indications that these drugs are likely to increase the pain and deformities in cases with neural forms of leprosy. For acute cases, dapsone is given by mouth. To avoid the possibility of very severe toxic effects it is advisable to begin with a small dose, as low as 25 mg. twice a week, gradually increasing at weekly intervals until 0 1 g twice weekly is reached. This [illegible]

be maintained for four weeks, then 0·2 g. is given twice a week for a further four weeks; thereafter it is raised to 0·3 g. twice a week. If the drug is well tolerated after twelve weeks, the dose may be increased to 0·4 g. twice a week or 0·1 g. daily. For children under six, one-quarter of the adult dose, and under twelve, half the adult dose, should be prescribed. Yeast and iron are given during sulphone treatment to correct any upset of blood formation.

Toxic effects, which are largely *avoidable by the above cautious regimen*, include anæmia, dermatoses, lepra reactions, neuritis, psychosis and hepatitis. The occurrence of any of these necessitates the temporary cessation of treat-

or in difficult cases

lution up to 2·5 g.

is reserved for

patients intolerant to the sulphones.

Cortisone may be required in severe lepra reactions and can be given with advantage in addition to solapsone, for a period, when chemotherapy is restarted. Hydrocortisone eye drops (1 per cent. solution) are of great value in the control of acute or subacute leprous eye reactions, which if unchecked lead to serious eye changes. The hydrocortisone solution should be frequently applied to the eye and continued until the inflammation has subsided, sulphone treatment being maintained at the same time During the acute stage of the process 1 per cent. *atropine drops are instilled into the eye morning and evening.*

In tuberculoid leprosy the tendency is towards arrest, but cure may be hastened and deformities prevented by early sulphone treatment. Treatment should be continued for a minimum of twelve months and for not less than six months after apparent cure. The clinical manifestations of lepromatous leprosy may be dramatically affected or respond extremely slowly, but in any case treatment must be continued for at least twelve months after negative skin smears are obtained. The patient must be prepared for treatment lasting for many years. Follow-up is essential, as relapses have occurred and their frequency is not yet known Physiotherapy and orthopædic measures are often necessary to correct deformities resulting from peripheral nerve involvement.

General Management.—A very important part of treatment is good food,

Personal Prophylaxis.—Children are very susceptible to leprosy, and mothers in countries where the disease is prevalent should not allow their children to run the risk of close or constant contact with infection. Adults, though less susceptible, should take reasonable precautions. Leper colonies, with facilities for treatment, are important for the prophylaxis of leprosy. Particular care should be taken to disinfect the nasal discharges of lepers and also their eating and drinking utensils. Contact with discharging lesions of the skin should be strictly avoided as these often contain very large numbers of bacilli. Washermen, cooks and other servants should be regularly inspected for any signs of leprosy.

YAWS

Specific Treatment.—The earlier methods of treatment by injections of bismuth and arsenical preparations are now being abandoned in favour of

treatment by penicillin. Procaine benzylpenicillin is effective. Treatment with 600,000 units given as a single injection and half this dose to other members of the family is undoubtedly effective. It is however generally agreed that 600,000 and 1,200,000 units in a single injection, for children and adults respectively, with half that dose for contacts, gives the best all-round results. The treatment of contacts is essential, and in an endemic area in practice this means treating the whole population. A re-survey is necessary, as a few relapses or further infections may occur, but the incidence of the disease, where the people co-operate, is rapidly reduced. Tetracyclines have been found to be equally effective, and when they become available at a reasonable cost, oral treatment should make possible the complete eradication of the disease.

General Management.—Sufferers from yaws are usually undernourished and this should be remedied if possible. Any helminthic infection should be treated.

Personal Prophylaxis.—Wounds and abrasions should be protected from flies or infected material.

YELLOW FEVER

Specific Therapy.—There is no specific treatment for this disease, and serum from convalescents, even if available, is of no value after symptoms have developed.

Non-specific Therapy.—The disease varies greatly in severity, from a mild attack with no recognizable symptoms to a very severe and rapidly fatal disorder with classic symptoms and signs. In severe cases, careful nursing of the patient, at complete rest in bed, is essential. As much fluid as possible should be taken containing the juice of citrus fruits and glucose. When vomiting is troublesome, 5 per cent glucose solution should be given intravenously, alternating with normal saline solution. To combat acidosis, 10 to 15 g. sodium bicarbonate or lactate can be given daily by mouth in divided doses, but where there is much vomiting 15 g. of sodium citrate in a pint of sterile water may be given intravenously. Anuria is a very serious complication; when this occurs the treatment recommended for anuria in blackwater fever should be employed (see p. 201). The application of an ice-bag to the head, or cold compresses, may give welcome relief when headache is severe. Should the temperature rise unduly, cold sponging should be employed.

Personal Prophylaxis.—Immunization with yellow fever vaccine is the most important method of personal prophylaxis. This must be carried out at least ten days before arrival in the yellow fever area. Two attenuated living strains of vaccine are now in use—the 17D strain produced in the chick embryo for subcutaneous injection and the French neurotropic strain administered by skin scarification, with or without the addition of vaccinia virus. There have been reports of serious encephalitis, especially in infants, following the scarification method, consequently this method is not recommended. The 17D vaccine consists of a suspension of attenuated living yellow fever virus which has lost its pathogenicity for man but retains its immunizing powers. It confers immunity for at least six years and can protect whole communities at risk against yellow fever, so that they do not suffer from nor carry the disease from yellow fever areas to places where potential mosquito vectors are abundant and the population completely unprotected. The vaccine is issued in ampoules in

Treatment of those who have been Exposed to Infection.—Careful local treatment of the bite is very important. The wound should be thoroughly washed immediately with soap and water. *Then it should be excised or opened*

When preliminary cleansing is efficiently done within thirty minutes of the bite,

Should it develop an illness during this period and die, or have to be killed, two portions of the brain from the region of the corpus callosum, one in formol saline and the other in glycerine, should be sent to an experienced pathologist for examination for Negri bodies. In this country, except in quarantine kennels, it is most unlikely that an infected dog will be found. Nevertheless, whenever the suspicion is strong, the Veterinary Authorities should be informed, either directly or through the police.

After the local treatment has been applied, if the person is considered to be definitely at risk, he should undergo a course of anti-rabies inoculations. Bites by any dog, etc., in an infected area, must be regarded as infective until proved otherwise, and immunization instituted immediately. Contact of the unbroken skir

hat have not drawn blood, on any part of the body except the head, face, neck or fingers. Licks on the intact mucous membrane.

Class II.—Moderate risk: licks on cuts or abrasions on fingers. Bites or scratches on the fingers less than a quarter of an inch long and not penetrating the skin Bites and scratches on all parts of the body, excluding the head, face, neck or fingers, that have drawn blood but are less than five in number and are without any extensive laceration

Class III.—Severe risk. *licks on abrasions and all bites and scratches on* head, face or neck Severe bites or scratches on fingers. Five or more bites drawing blood anywhere. All extensive lacerations All jackal and wolf bites *All cases in Class II where treatment has been delayed over fourteen days.*

In view of the rare possibility of neuro-paralytic accidents being sustained by a person who in retrospect was shown to have been in contact with the suspected dog, people in Class I should await the death of a confined suspected dog before commencing treatment.

Vaccines.—There is a great variety of vaccines used for anti-rabic inoculations in different countries. Essentially they all consist of a suspension of animal nervous tissue containing the fixed virus of rabies. The virus may be either living (but attenuated) or killed. The latter is the type more generally used today, but both the method of preparation and the dosage recommended vary considerably. Detailed instructions are issued with every ampoule of the vaccine issued.

The vaccine is given subcutaneously into the abdomen in different areas each day. If the dose is more than 5 ml. *for an adult or 2 ml. for a child, it is given*

in divided doses in two areas. The patient lives quietly during treatment and avoids alcohol. The immunity conferred lasts only three months.

Local allergic reactions occur and occasionally an abscess develops due to sepsis. Neuro-paralytic accidents have occurred, especially after the use of living vaccine These usually appear between the tenth and fifteenth day of treatment and are generally considered to be due to anaphylactic hypersensitivity related to the animal nervous tissue used in the inoculation They may present as mono- or polyneuritis, Landry's paralysis and transverse myelitis or, less frequently, as an encephalitis

In recent controlled therapeutic trials when hyper-immune serum was used along with vaccine, nine out of ten patients at " severe risk " survived. The combination of this serum with the usual vaccinations is especially indicated in such cases, as after vaccine alone antibodies do not appear for fourteen days or more. When serum is given, antibodies are present at once and persist, especially in those who have been given two doses. The first dose, 0·5 ml. per kg body-weight intramuscularly, is given as soon as possible after the bite, the second after four days Where the risk of infection is great, then the serum may have to be given more often, at shorter intervals and for a longer period. Anti-rabic serum is available commercially (Lederle)

Personal Prophylaxis.—In a country where rabies is a risk, all suspected animals should be avoided Dogs showing signs of choking should be handled with great care, as this is often the first sign of rabies. Fingers should never be put into the mouth of the dog. It is important and easy to protect dogs by a single injection of a living chick embryo vaccine (Flury) once a year. Wolves and jackals and other infected animals should be destroyed. Where the vampire bat is the vector these creatures must be destroyed, and cattle protected by chick embryo vaccine.

PRICKLY HEAT

[illegible]

abo

late

clusion that frequent washing with soap and water deprives the skin of its sebaceous secretions and predisposes, in the first instance, to the formation of a keratin ring around the orifice of the sweat ducts This prevents the free escape of sweat, some of which infiltrates the superficial layers of the epidermis and causes a secondary reaction in the affected skin. A further stage of the skin lesion is reached when the sweat pores become blocked by large plugs of concentrically arranged keratin. Then the sweat ducts become distended and dis-

[illegible]

the keratin plug and allows the sweat to escape to the surface

The deficiency of skin lipoid may be brought on by friction of hot sweat-saturated clothes and the frequent use of alkaline soaps and hot water. Natural

Treatment of those who have been Exposed to Infection.—Careful local treatment of the bite is very important. The wound should be thoroughly washed immediately with soap and water. Then it should be excised or opened

some infections are prevented and in others the incubation period is prolonged, enabling immunization to become effective.

A dog which has caused a bite and is suspected of being rabid should not be killed but be kept securely tied up, with two collars and chains, and observed for ten days. If alive and well then, it was not infective at the time of tying up Should it develop an illness during this period and die, or have to be killed, two portions of the brain from the region of the corpus callosum, one in formol saline and the other in glycerine, should be sent to an experienced pathologist for examination for Negri bodies In this country, except in quarantine kennels, it is most unlikely that an infected dog will be found. Nevertheless, whenever the suspicion is strong, the Veterinary Authorities should be informed, either directly or through the police.

After the local treatment has been applied, if the person is considered to be definitely at risk, he should undergo a course of anti-rabies inoculations. Bites *by any dog, etc., in an infected area, must be regarded as infective until proved* otherwise, and immunization instituted immediately. Contact of the unbroken skin with saliva of a rabid animal does not constitute an exposure.

Risks are classified as follows:

Class I.—Slight risk: licks on abrasions, bites or scratches that have not drawn blood, on any part of the body except the head, face, neck or fingers. Licks on the intact mucous membrane.

Class II.—Moderate risk: licks on cuts or abrasions on fingers. Bites or

without any extensive laceration

Class III.—Severe risk. licks on abrasions and all bites and scratches on head, face or neck. Severe bites or scratches on fingers. Five or more bites drawing blood anywhere. All extensive lacerations All jackal and wolf bites. All cases in Class II where treatment has been delayed over fourteen days.

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embryo vaccine.

PRICKLY HEAT

As the cause of prickly heat is still uncertain, it is not possible to be dogmatic

that the affected skin is deficient in fat and its replacement by lanoline softens the keratin plug and allows the sweat to escape to the surface.

The deficiency of skin lipoid may be brought on by friction of hot sweat-saturated clothes and the frequent use of alkaline soaps and hot water. Natural

world where infestation of the pig with cysts of *T. solium* is common A patient harbouring *T. solium* in his intestine should be treated as soon as possible, since he may ingest the eggs following contamination of his hands and thus acquire cysticercosis. In the East the normal intermediate host of *T. solium*, the pig, is often infested. There, pork should not be eaten unless it has been obtained [illegible]

food

Hydatid Cyst

This condition represents the larval stage of the small tapeworm, Echinococcus granulosus, which lives in dogs as the definitive host; man is an intermediate [illegible]

symptoms surgical removal of the cyst and its laminated membrane may be required. Care must then be taken to prevent the implantation of further cysts during the operation. Scolices can be destroyed by washing out the hydatid cavity with 1 200 formalin solution. The residual cavity may have to be marsupialized. Cysts in a long bone usually call for amputation. Antibiotics are useful in the control of secondary pyogenic infection

Personal Prophylaxis.—Close contact with sheep-dogs, the hosts of the adult worm, must be avoided. It should not be forgotten, however, that hydatid disease, which is by no means a rare condition in this country, may date back to infestation many years before the frank condition presents itself. The use of a reliable antigen for the intradermal test or the complement fixation test is a valuable aid in diagnosis when signs and symptoms point to this condition. A positive intradermal reaction is given in over 85 per cent of infested persons, but this may occur with dead cysts and persist for years after removal of live cysts Cross reaction occurs in the presence of infestation by other tapeworms. The complement fixation test is positive in over 80 per cent of infected persons, this titre soon falls after removal of the hydatid. A cross reaction with cysticercosis must be excluded in interpreting results. After handling sheep whose wool may be infected, the hands should be carefully washed especially before eating.

treatment has been completed. The usual course of treatment with diethylcarbamazine is 2 to 6 mg. per kg body-weight daily, given in three divided doses after food, for a period of three weeks.

It is advisable to start with a small initial dose, as this diminishes the tendency to allergic reactions which result from destruction of the microfilariæ. Even with this precaution, however, fever, pruritus, headache, arthralgia, malaise or nausea may be very troublesome. Some relief to these symptoms is afforded

of microfilariæ in the cerebral tissue These reactions are unusual when the initial dosage has been kept small, they can be controlled by antihistamine drugs and where severe by cortisone.

In *W bancrofti* infestation the most satisfactory results are achieved when treatment has been started early before obstructive lesions have occurred, even in the late cases, however, improvement may result In long-standing elephantiasis surgical measures are required to improve the lymph drainage and remove redundant tissue Antibiotics and oral sulphonamides are useful for the pyogenic infections which probably play a considerable part in the symptomatology of these filarial lesions In loiasis the adult worm occasionally passes under the conjunctiva, whence it can be removed the technique is described in manuals of tropical medicine

Onchocerca volvulus often causes intense itching and produces a thickening and infiltration of the skin with loss of elasticity Small subcutaneous tumours may also be found in various parts of the body, those about the head are often associated with ocular lesions which may progress to blindness These tumours have been removed under local anæsthesia to lessen the likelihood of eye damage; better results are now being obtained by treatment with suramin The recommended treatment with suramin is 2 mg. per kg body-weight—five doses at weekly intervals up to a maximum of 5 g The initial dose is a quarter of the normal weekly dose Suramin kills the adult *O volvulus* and is less likely to produce the severe allergic phenomena induced by diethylcarbamazine which may lead to serious aggravation of the eye lesions Where the vision has been impaired, definite improvement has been reported following a course of suramin. This treatment also relieves the cutaneous manifestations of onchocerciasis and is less likely to cause the troublesome side-effects—pruritus, urticaria and pyrexia—which occur with diethylcarbamazine treatment It should therefore be employed as the initial therapeutic measure in this disease and diethylcarbamazine only used later if required

Personal Prophylaxis.—This consists in measures against the vector of the particular filarial worm Certain species of mosquitoes are responsible for the spread of *W bancrofti* and *W. malayi*, and measures of personal protection as detailed under malaria should be carried out The vectors of *Loa loa* are various species of mango-fly—including *Chrysops dimidiata* and *C. silacea*—

lines employed against mosquitoes are of value against this vector. A dose of diethylcarbamazine every three months reduces the infectivity of the population. Mass treatment over a period of seven days is even more effective.

Dracunculus medinensis or Guinea worm. The adult female is found in the subcutaneous tissue, generally of the leg. Treatment depends on the stage at which the patient is seen Diethylcarbamazine has been reported as effective against immature forms of dracunculus and in maximal doses even against the adult worm. The early toxic anaphylactoid symptoms are best treated by injections of 0 6 ml (10 min.) of 1 : 1,000 adrenaline solution, or by one of the antihistamine drugs such as mepyramine maleate and by aspiration of the blister if present. When an ulcer has appeared, it should be kept as clean as possible and the worm removed by gentle intermittent traction and massage. Alternatively, the worm may be removed by incisions along its course, under a local anæsthetic. Should local infection occur with abscess formation, this must be treated on surgical lines.

Infection is contracted from drinking-water containing infected cyclops (water flea), the intermediate host, cyclops; they are also readily kill source of danger, those used for so that water is drawn from above.

ANCYLOSTOMIASIS

Specific Treatment.—Tetrachlorethylene or hexylresorcinol crystoids (Sharpe and Dohme)

The vermicidal effect of the drug is greatest when the upper bowel is empty. The hexylresorcinol or tetrachlorethylene is therefore given after the patient has fasted overnight.

stored in a cool dark place.

Hexylresorcinol crystoids kill intestinal nematodes, including *Ascaris lumbricoides* and hookworms, but the drug does not usually reach them all As a result, repeated treatment may be required. Fasting is arranged as above; the adult dose of hexylresorcinol crystoids is five 0 2 g capsules on an empty stomach followed by a saturated sodium sulphate solution ... The treatment may be ... year of age ... chews the capsule, superficial erosions of the buccal mucosa may occur.

Non-specific Treatment.—The irritation of ground itch can be relieved by the application of an ointment containing zinc oxide and salicyclic acid Anæmia associated with a hookworm infection responds well to treatment with iron in adequate doses. A well-balanced diet, containing meat and vegetables, is desirable if obtainable. Where the anæmia is extreme, it should be corrected with iron before beginning anthelmintic treatment

ASCARIASIS

Specific Treatment.—The treatment for ancylostomiasis is also effective against *Ascaris lumbricoides*. The piperazine preparations are, however, more effective. Piperazine citrate (Antepar) is non-toxic and gives excellent results

in ascariasis. The adult dose of the syrup is 24 ml., which contains 3 g. of piperazine citrate; for a child under 20 kg., 16 ml. is a suitable dose. This is given as a single dose before the evening meal followed by a saline aperient next morning to expel the worms. Piperazine adipate (Entacyl) is put up in tablets of 0·3 g.; it is equally effective given in doses of 0·75 g. for each year of life up to six years, and 4·5 g. from six years upwards. This treatment is taken in four divided doses after meals during one day without any special preparation or dieting and followed by a mild saline aperient next morning. Good results have also been reported with piperazine adipate given over a three days' period. In rare cases very large collections of worms may cause intestinal obstruction necessitating surgical intervention.

Personal Prophylaxis.—In areas where infection is common, uncooked vegetables and other raw food should be avoided. The hands should be carefully washed before meals.

STRONGYLOIDIASIS

Infestation with *Strongyloides stercoralis* is common in the tropics and subtropics and is especially prevalent in the Far East. It may produce chronic diarrhœa and occasionally cutaneous irritation.

Specific Treatment.—Gentian violet, as used in the treatment of threadworms (see Enterobiasis), has been employed in this infestation, but the results are disappointing. It has been given by intubation and intravenously with inconstant results.

Personal Prophylaxis.—As for ancylostomiasis.

ENTEROBIASIS

If one member of a family has threadworms, the rest of the family and associates should be suspected and treated simultaneously. The N.I.H. (U.S. National Institute of Health) cellophane swab, which is a small piece of cellophane tissue over the end of a glass rod or similar article, is a useful way of detecting infestation. By rubbing the cellophane firmly over the anal region and subsequently examining this spread out on a moist slide, eggs can be detected with the low power of the microscope. When an infestation is discovered in a house, it is essential to investigate all members of the household.

Specific Treatment.—The most effective specific treatment for threadworm is piperazine citrate (Antepar) or piperazine adipate (Entacyl). The dose of the former is 50 mg. per kg. body-weight daily, taken in divided doses morning and evening. A two weeks' course is advised with an interval of seven days at the end of the first week. The course of piperazine adipate is given over a period of a week; it consists of one tablet (0·3 g.) per year of life per day up to the age of six years and over six years 2 tablets three times a day, given in divided doses. The need for simultaneous treatment of all members of the family should be remembered.

General Management and Personal Prophylaxis.—It is very important to prevent reinfection with ova; nails should be kept short and hands washed carefully, especially before meals. Close-fitting sleeping-drawers and gloves should be worn at night. All possibly infected clothing, linen and towels should be boiled daily. The anal region should be smeared before bedtime with

ammoniated mercury ointment. By adopting these precautions the risk of reinfection with ova will be minimized.

TRICHURIS TRICHIURA

Fortunately this worm does not give rise to any serious lesions. It is very difficult to dislodge by any known anthelmintic treatment. Recently piperazine adipate has been used in dosages as for enterobiasis but a controlled experiment has failed to demonstrate its value.

TRICHINIASIS

There is no specific treatment for an established infestation with *Trichinella spiralis*, but the administration in the early stages of tetrachlorethylene followed [illegible] ition and so lessen the number [illegible] treatment is symptomatic.

[illegible] the infestation to pigs, access of rats to pigsties should be prevented Although gross infestation of pork should be obvious if proper examination of meat is undertaken in the slaughterhouses, infested carcasses do escape detection. It is essential, therefore, that all pork should be more thoroughly cooked than other carcass meat and this applies especially to pork sausages. Outbreaks of trichiniasis have frequently been traced to the consumption of partially cooked pork sausages. Bear meat, an article of food in some countries, may be similarly infested.

INSECTICIDES, REPELLENTS AND ACARICIDES

Insecticides.—A wide range of chemicals is used against arthropod pests in agriculture as well as against insects of medical importance In the past, substances of vegetable origin such as pyrethrum, extracted from the flower heads of chrysanthemum, were used mainly in sprays and powders against mosquitoes, flies, fleas and lice because they acted quickly and were relatively harmless to mammals. Inorganic minerals such as arsenicals and fluorides, acting mainly as stomach poisons, and organic minerals such as naphthalene, phenol, cresol and kerosene, have also been used to kill insects. All these have some disadvantages, being either harmful to mammals, chemically unstable, available only in small quantities or very expensive to produce. Some are inflammable or have undesirable smell or colour. Progress towards the production of the ideal insecticide was made by the discovery that chlorinated hydrocarbons have great insecticidal powers.

Dicophane (DDT), dichloro-diphenyl-trichlorethane, the first of such synthetic products was discovered to have good insecticidal properties by the Swiss about 1939 It can be made from relatively simple chemicals ; it is specifically toxic to arthropods while having only slight toxicity to vertebrates. It is free from [illegible]

unaffected by light, air or water.

DDT in minute concentrations is lethal to larval and adult forms of mosquito, to the adult house-fly, to the larval stages and to adult lice, and to many other insect vectors of disease. The exact method of action of DDT is not known, but when it comes in contact with an insect's cuticle it penetrates the cuticle, diffusing in the lipoids of the nervous system. It gives rise to paralysis which gradually becomes widespread, leading to death of the insect The action of the poison is slow and insects sometimes recover if they have received only a very small dose. Although primarily a contact poison, it may act as a stomach poison too. If handled with reasonable care DDT is innocuous to human beings, but

DDT dust and prolonged inhalation may produce toxic effects including severe

important measure in plague control. DDT may be used as Dicophane Application (BPC) against head lice—it must be remembered that DDT has no action against eggs, so that application should be repeated to ensure that larvæ

sprayer. DDT may be used in solution or emulsion, sprayed directly at insects for domestic control of insect pests Such sprays are designed mainly against house-flies and mosquitoes DDT is rather slow acting and so pyrethrum (0 03 per cent. pyrethrin plus 5 per cent. DDT) should be added to obtain a quick knock down.

Recently allethrin, a synthetic product acting just as pyrethrum does, has been introduced A convenient form of using space sprays is the ærosol "bomb". The insecticide (DDT+pyrethrin) is dissolved in a liquified gas, and when pressure is released an atomized spray of insecticide is emitted Ærosols have only a transient effect, either drifting away or falling to the ground within ten to thirty minutes, but if the doors and windows are kept closed, this suffices to clear a room of flies

When DDT in a suitable volatile solvent is sprayed on to a surface, the solvent evaporates and leaves a fine film of DDT crystals A surface so treated

inch. The nozzle should be held about two feet from the surface to be sprayed and the whole surface covered with insecticide so as to leave it moist but not dripping. Windows and doors are kept closed during spraying; foodstuffs should be protected from the spray, but furniture should not be removed. This so-called residual spraying is effective against flies, fleas, bed-bugs, mosquitoes

and sandflies A 5 per cent solution of DDT in kerosene or Malariol applied to the surface of mosquito-breeding areas will kill all larvæ within a few hours and will also destroy pupæ One quart of a 5 per cent solution is sufficient for one acre of water surface. Balls of plaster of Paris or bricks soaked in the solution for twenty-four hours may be thrown into breeding-places to provide [illegible]

by insects on contact, but its action is quicker. It is much more toxic to insects, so that it may be used in a concentration of about one-tenth of that necessary with DDT. Gamma BHC is toxic to ticks, whereas DDT is not. Pure gamma BHC is a white crystalline substance insoluble in water but soluble in many organic solvents. It has a rather pungent and objectionable odour in all but the purest preparations. It has a small vapour pressure which makes it less persistent than DDT although the vapour it gives off is insecticidal. The method of application of gamma BHC is the same as for DDT—that is, as powder, dispersible powder, solution and emulsion. BHC smoke-generators spread the [illegible]

BHC is only slightly toxic to mammals, but reasonable precaution should be taken as in the handling of DDT.

Diels-Alder Condensation Products—Chlordane, heptachlor, aldrin and dieldrin have been synthesised since 1945. Dieldrin seems to be the most promising member of this group It has the prolonged residual effect of DDT and the high insecticidal powers of gamma BHC. It is more toxic to mammals, but if adequate precautions are taken the hazard is not great. Dieldrin may be applied as a powder, as solution, as a wettable oil or emulsion, or, in anti-larval measures, as granules. These granules of bentonite clay coated with dieldrin can be dispersed in mosquito-breeding places and they gradually release toxic amounts of the insecticide over a considerable period.

[illegible] ed as a lacquer to wood-wor[illegible] elve mo[illegible] the lacquer and crystallizes there so that the surface may be rubbed down and cleaned, but crystals removed in this way are replaced by crystals coming to the surface from within the lacquer.

Organo-phosphorus compounds such as parathion and schradan were developed in Germany They are highly toxic to arthropods and vertebrates. Their characteristics make them very suitable for agricultural pest control, but because of their dangerous nature they are considered unsuitable for use against pests of medical importance. The Agriculture (Poisonous Substances) Regulations, 1954, lay down the precautions necessary to protect employees against the risk of poisoning by the organo-phosphorous and dinitric compounds when used in agriculture.

Resistance.—Some strains of house-flies, certain culicine mosquitoes and some strains of body-lice have developed the ability to withstand doses of insecticide which would kill the average members of the same species Cross-

in febrile conditions the food intake should be diminished as regards fat, but an adequate supply of carbohydrate in the form of cane sugar or glucose is to be recommended. These principles can be put into practice by using one of the half-cream dried-milk preparations or by diluting liquid milk to half strength

unusual for a well-nourished infant weighing, say, 12 lb to lose 8 oz. (i e. one-twenty-fourth of his weight) in the first twenty-four hours of an acute diarrhœal disease This loss of weight is almost entirely accounted for by loss of fluid from the blood and tissues So prone is the young child to become dehydrated and so evil are the consequences that it is frequently necessary to give fluid by routes other than by the mouth (see p 113)

Drugs.—The administration of drugs is often difficult It is better to give them in solution rather than as powders It is impossible to give pills unless

adult dose$\times\frac{\text{age}}{\text{age}+12}$. Using such a formula there is little if any likelihood of overdosage, but there are many drugs which may be given in much larger doses than the use of the formula would suggest—e g chloral hydrate, belladonna and its active principle, atropine, and calcium or ammonium chloride. Preparations containing strychnine as well as opium and its derivative, morphine, must be given with caution The most useful sedative for young children is chloral hydrate. It is particularly safe and has no cumulative effects. Acetyl-salicylic

The most useful laxatives are fluid magnesia, syrup of figs and paraffin preparations; the use of mercurials such as mercury and chalk cannot be recom-

held in the right hand well into the back of the mouth In order to get him to swallow, it is sometimes necessary to compress the nostrils for a few seconds.

SPECIAL METHODS OF FEEDING

Sometimes on account of grave debility or because of deformity of the lips and mouth (hare-lip and cleft palate) the infant is unable to suck either the breast or the bottle. In these circumstances special methods must be employed The commonest of these is spoon-feeding This is often invaluable although time-consuming. Another method is to give the food by a pipette to which a small

SOME COMMON DISORDERS IN INFANCY AND EARLY CHILDHOOD

INTRODUCTION

ACUTE INFECTIONS are more common in children than in adults, and are often fraught with more serious consequences. At the same time children have remarkable powers of recuperation, and once the acute phase of infection is overcome, convalescence is as a rule rapid. Despite the extensive use of sulphonamides and antibiotics, general measures are still of paramount importance · these include good nursing, the giving of a suitable *diet and the administration of a plentiful supply of fluid ; the irritable, sleepless infant may require a sedative, and in other circumstances cerebral stimulants* may be needed.

The sick infant should, where possible, have a room to himself and on no account should a bed or cot be shared. The temperature of the room is best kept between 60° and 65° F. The child's clothing should be loose and comfortable. Harsh woollens next the skin are often irritating. After the umbilical stump is healed, a binder is no longer required ; it impedes respiratory movement and is also a source of skin irritation Great care should be taken to prevent skin infection ; a sweat rash which would not be more than a source of irritation in the adult may lead to widespread and serious skin infection in the infant. *Frequently it is necessary to prevent a child from scratching or picking at an* infected area on the skin. To accomplish this the arms should be splinted so that the elbows cannot be flexed. The best method of doing this is to bandage strips of cardboard to the arms, extending above and below the elbow. The [illegible] removed at night. The buttocks [illegible]

which can be thoroughly [illegible] gastro-intestinal upset, ordinary cow's milk may be used in their diet, but for *the first four years at any rate* it should be heat-sterilized. Generally speaking,

cannot as a rule retain more than 60 ml. (2 fl. oz.) at a time. When there is diarrhœa or rectal irritation this method of giving fluid should be avoided.

Subcutaneous Route.—This is the simplest of the three methods of giving

given slowly by the continuous drip method, little or no pain is caused and as much as 500 ml. can be given in twenty-four hours Hyaluronidase, 1 to 2 mg. per litre of infused fluid may be injected subcutaneously at the site of the insertion of the infusion needle to increase the rate of absorption.

Intravenous Route.—This is the most direct, rapid and effective method of giving fluid, and in modern hospital practice has replaced the other routes. The principles involved are similar to those obtaining in the adult Veins in infants are much smaller, however, and it is frequently necessary to expose a vein under local anæsthesia and to tie in a small metal cannula (a Bateman's or Hamilton-Bailey needle is often used), or polythene tubing (No. 1) can be threaded over a small needle before insertion For this the internal saphenous vein, as it crosses the internal malleolus, will be found suitable. Employing very

anæmia, the intravenous drip is often a life-saving measure

In infants in whom the anterior fontanelle is still patent, fluid may be

in our experience the method is free from risk The technique is as follows: the child should have his arms pinioned by being firmly wrapped in a blanket

minutes.

NEO-NATAL CONDITIONS

Prematurity.—A premature infant is defined as one whose birth weight is 2 5 kg. (5½ lb.) or under. As prematurity accounts for at least half the

piece of rubber tubing has been attached. The food can be introduced drop by drop into the back of the throat. For the child too weak to swallow or for one

funnel connected by rubber tubing and a short glass connecting piece to a small stomach tube (No. 8 to 10, English). The tube is lubricated with glycerin and inserted through the mouth into the stomach. A rough estimate of the length of tube to be passed in order to reach the stomach may be obtained by measuring the distance from the mouth to the xiphisternum. The tube is then marked by a *thread tied round it at the appropriate distance from its point. After the* tube has been inserted, any residue of food lying in the stomach is withdrawn by siphonage and the food is then run into the stomach. The tube should be withdrawn slowly and compressed between the finger and thumb to prevent reflux into the larynx. This is particularly important when dealing with premature and feeble infants.

A similar apparatus *may be employed for gastric lavage. The fluids used for this are normal saline solution or a solution of bicarbonate of soda, a teaspoon*ful to the pint of water.

SPECIAL METHODS OF GIVING FLUID

Extra fluid may be given to infants by the rectum, although in diarrhœal conditions this is useless as it cannot be retained and may act as an irritant. Fluid may also be given parenterally, i.e by routes other than the alimentary tract, such as into the subcutaneous tissues, *the peritoneal cavity or a vein.* Administration of fluid by injection into the bone marrow has also been advocated. The tibial marrow is used and special needles are made for this, but the grave consequences of infection make this method undesirable. The intraperitoneal route enjoyed considerable popularity in past years, but is now seldom used and will not be described.

Parenteral fluid is best given as plasma or as half-strength physiological saline (quarter-strength in *the newborn infant) with the addition of 5 per cent.* glucose. Plasma substitutes such as Plasmosan or dextran can also be recommended if fresh plasma is not available. Full-strength physiological saline is apt to cause œdema in young infants. Recently the advantages of adding sodium lactate and/or potassium chloride to the infused fluid have been stressed.

culatory

failure. (See p. 113)

Rectal Administration.—A rubber rectal tube (size No 10) to which a funnel is attached is, after lubrication, gently inserted into the rectum to a

should be held together for a few minutes after withdrawal of the tube. This procedure may be repeated after an interval of four hours Young infants

jacket with hood to cover the head and overlapping in front Instead of a napkin

e must be taken to prevent burns. An especially in institutions, but it should always be covered by some non-conducting material such as rubber and placed over, not under, the infant. The weight of the insulated blanket is supported by a cradle. The infant should have a cubicle or room to himself with ample warm, moist air: in the home the humidity of the air can be conveniently increased by placing a bowl of hot water near an electric fire or by using a kettle. The temperature in the infant's cot should be at least 90° F. at first, although the room temperature can be kept at about 80° F. A humidity of 65 to 70 per cent. is recommended

Every possible care should be taken to prevent infection. Skin abrasions, if present, should be treated twice daily with a 1 per cent aqueous solution of

If there is no œdema and the infant is strong, and if breast milk is available, he should be put to the breast in the usual way. If he is small, too weak to suck, and especially if there is œdema present, it will be found advisable to delay all feeding, even of water, for twenty-four to forty-eight hours and occasionally longer; at the end of this time it is usually found that he will suck reasonably well. This is of great advantage in that gavage and its attendant risks of inhalation pneumonia are avoided. The use of pipettes and Breck feeders should also be avoided as much as possible and for the same reasons.

The feeding of the infant is greatly simplified if breast milk is available, and every attempt should be made to procure this. Modern practice is to have in every community a "breast milk bank"—usually at the local maternity hospital, where breast milk can be stored and dispensed as required All such expressed breast milk fed to premature infants should be boiled. Failing breast milk, one of the half-cream dried milks (half-cream Cow and Gate, No 1 Ostermilk, half-cream National Dried Milk) may be used The heavier premature infants may be given four-hourly feeds of 1 oz (30 ml) of the reconstituted dried milk to which half a teaspoonful of sugar has been added. In the smaller babies as little as 5 to 15 ml. may suffice as the initial feeds and should be given three-hourly. Only in exceptional circumstances is it advisable to feed an infant more often.

Premature infants are prone to develop rickets and hypochromic anæmia. It is important that steps be taken to prevent such deficiency states. Because of their rapid growth, it is now recognized that these infants require more vitamin D than full-term infants—about 1,400 international units daily instead of 700

calciferol B.P., two or three drops (1,000 to 1,500 units), or one of the proprietary preparations (see N.F) are equally satisfactory. When using a concentrated preparation, measured in drops, it is well to instruct the mother to

neo-natal mortality, the care and treatment of these small infants is a matter of great importance and responsibility. The ideal treatment is prevention, but in about half the cases no cause of the prematurity can be found. There is considerable evidence that an inadequate diet, especially during the last three months of pregnancy, increases the likelihood of premature birth. Its incidence, too, is greatest among mothers of poor physique and who are living in conditions of poverty and squalor. The prevention of prematurity is therefore a national problem linked up with the general health of women of child-bearing age and their economic position. Under present conditions, good ante-natal care, using the term in its widest sense, is the most important factor in the prevention of premature births

The chance of survival in any given case depends mainly on the weight of the infant at birth and on the presence of disease or injury. With experienced nursing skill and attention to detail much can be done even for very small and weakly babies

If the mother is delivered at home, the decision as to whether the infant can be adequately cared for there or requires transfer to hospital is one that must be taken early. This is dependent on the social and economic circumstances, the help available, and whether or not there is a special unit in the vicinity for the care of premature infants.

In all districts there should be such a unit, preferably attached to the maternity hospital, where premature infants can receive treatment Doctors and nurses with appropriate training should be in charge. Most premature infants under 3½ to 4 lb. probably require hospital treatment and there should be adequate arrangements for their transport. In such units very small infants are often nursed in the nude state in incubators with regulated temperature and humidity. As soon as breathing is well established (usually in a few hours), the head may be raised by altering the plane of the mattress This makes it easier for the weakly infant to breathe , the nude state is preferred for the same reason.

pneumonia.

No matter what the circumstances, if it is suspected that the infant will be small, special preparations should be made for his reception. A cot or bassinet with the necessary blankets and hot-water bottles must be in readiness, and if

obstructed. They may be cleared by the use of a mucus extractor, which should be readily available at all times. (Attempts to remove mucus by the finger wrapped in gauze are ineffective and dangerous.) The infant should then be

approved methods (see Asphyxia), care being taken to ensure that the percentage in the tent or incubator, whichever is used, never rises above 40 per cent. measured by a gauge. The period of administration should not exceed two or three days. It is not necessary to give extra oxygen to all infants in incubators.

The infants should not be bathed : later on, the skin may be cleansed using warm sterile olive oil. A single garment is used : it consists of a sleeveless

jacket with hood to cover the head and overlapping in front. Instead of a napkin

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In all districts there should be such a unit, preferably attached to the maternity hospital, where premature infants can receive treatment. Doctors and nurses with appropriate training should be in charge. Most premature infants under 3½ to 4 lb probably require hospital treatment and there should be adequate arrangements for their transport. In such units very small infants are often nursed in the nude state in incubators with regulated temperature and humidity As soon as breathing is well established (usually in a few hours), the head may be raised by altering the plane of the mattress. This makes it easier for the weakly infant to breathe ; the nude state is preferred for the same reason Clothing of any kind, and especially a binder, impedes respiration. With careful management along these lines many infants in the group with birth weights of 3 to 4 lb. survive who would otherwise fall victims to asphyxia and inhalation pneumonia.

No matter what the circumstances, if it is suspected that the infant will be small, special preparations should be made for his reception. A cot or bassinet with the necessary blankets and hot-water bottles must be in readiness, and if possible someone detailed to look after the infant as soon as he is born

If cyanosis is present or attacks of cyanosis are occurring, artificial respiration should not be attempted, but one must make sure that the air passages are not obstructed. They may be cleared by the use of a mucus extractor, which should be readily available at all times. (Attempts to remove mucus by the finger

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blood clot from the bowel must be dealt with promptly by warmth, quietness and injection of suprarenal cortex B.P.C. (1 ml.).

In mild cases, or in those for whom transfusion cannot be arranged, one of the analogues of vitamin K (menaphthone) should be used. It can be given

whole blood in 10 to 20 ml. amounts should be injected subcutaneously in the loose tissue between the scapulæ and repeated in four hours Grouping of the

guide, but the general condition of the patient is equally important.

Hæmolytic Disease of the Newborn (Erythroblastosis Fœtalis).—The primary fault in this condition is an acute hæmolysis of the infant's red cells due to the presence of antibodies derived via the placenta from the mother's blood. Although there may be other factors as yet undiscovered, the common

two.

All mothers should have their blood tested early in pregnancy, and if *presence of antibodies.* If

ll be affected and arrange-
e cord is cut, a sample of
the cord for the Coombs'

care must be exercised in collecting the sample of blood to avoid contamination with Wharton's jelly It must also be remembered that there is a danger in depending too much upon one single laboratory estimation. In deciding upon the correct management, the whole clinical picture must be considered, such as the presence or absence of jaundice, bile in the urine, enlargement of the spleen and evidence of hæmolysis in the peripheral blood. If there is anæmia but no jaundice, a straight transfusion may be sufficient, but opinion is gradually coming round to favour replacement transfusion as routine treatment in the first twenty-four hours as the red cells in the infant's blood are due to be destroyed and it is probably better to remove them at once and replace them with Rh-negative cells which will be unaffected by the antibodies. It should not be forgotten that when the father is heterozygous, a rhesus negative and therefore unaffected infant may be born to the mother of a previously affected child; in such a case there may be a deceptive rise in the maternal antibodies during pregnancy (anamnestic rise)

The Technique of Replacement Transfusion.—The umbilical stump is cut across about half an inch from the abdominal wall and a polythene catheter passed up the umbilical vein following the twist of the cord and through the abdominal wall. The catheter fills with blood which can be withdrawn by

syringe. Twenty ml. are withdrawn and discarded and 20 ml. of Rh-negative blood injected This procedure is followed until 300 to 400 ml. are withdrawn. An excess of 50 to 100 ml. of blood should be given. The technique, once acquired, is not difficult There is some danger of air embolism and heart failure.

Birth Injuries.—Birth injuries are extremely common, and, when involving the central nervous system, often serious. Their early recognition is most important if the best results from treatment are to be obtained

A cephalhæmatoma which consists of an effusion of blood beneath the pericranium of one of the flat bones of the skull is often a cause of considerable apprehension to the mother. Any attempt to remove the blood clot by aspiration or by incision is to be condemned. The risk of infection is too great If left untreated, such swellings disappear in two or three months and leave no traces. Despite conservative management a cephalhæmatoma may become infected, and in such circumstances should be dealt with surgically

The commonest sites of *fracture* in the newborn are clavicle, femur and humerus. Displacement may be great, but in otherwise healthy infants healing readily occurs without deformity Fractures of the clavicle require no special treatment, indeed probably only a small percentage of them is recognized. For the fractured femur a band of adhesive tape, 2½ in wide, is bound around the site of the fracture and the infant suspended by the legs from a light bar placed across the upper rail of the cot so that the buttocks are just free of the mattress. The weight of the child suffices to overcome any slight muscle spasm and produce satisfactory alignment Another method is to flex the thigh on the abdomen and fix it there with adhesive plaster The advantage of this method is that the child can be removed from the cot in order to be breast-fed or cleansed The limb should be kept fixed by one or other of these methods for a fortnight or three weeks and free movement can then be permitted The fractured humerus should also be bound up with a band of adhesive tape and the arm bandaged across the chest for a fortnight It has been claimed that without any immobilization such fractures heal well and that good alignment is obtained, but the infant will be made more comfortable if some simple form of fixation is used. Before fixing fractures of long bones the skin should be bathed with spirit and thoroughly powdered, special attention being paid to the axilla, antecubital fossa and groin.

True fractures of the skull are comparatively rare Gutter or funnel-shaped depressions of the skull bones, however, are not uncommon and are usually found in the antero-lateral part of the cranium There have been many suggestions for dealing with such conditions surgically, but they are much better left alone. The deformity, unless it is very severe, will disappear during the first year and the normal contour of the skull will be restored.

Asphyxia is the commonest cause of death in the neo-natal period It is so frequently associated with cerebral trauma, especially in premature infants, that it is impossible to define the two conditions as separate clinical entities. Each may be the cause of the other; and each may result in intraventricular hæmorrhage—which is usually fatal Among the manifestations are cyanosis (asphyxia livida) or attacks of cyanosis, inability to suck, a shrill cry, convulsions, a tense fontanelle and fever If the asphyxia persists, a state of shock (asphyxia pallida) supervenes.

Having made sure that the air passages are clear, the infant should be placed

Parasitic Stomatitis (Thrush).—This infection by *Candida albicans* has shown a sharp rise in incidence and is especially common in institutional nurseries for newborn infants. The condition is speedily remedied by dropping into the infant's mouth 1 ml. of a 1 per cent. aqueous solution of gentian violet thrice daily for three days. The dye will be well distributed over the mucous membranes in this way and some will be swallowed, which is of advantage because it protects the œsophagus. Recurrence and re-infection must be watched for. *Alkaline mouth-washes and applications of glycerin and borax are ineffectual.*

Aphthous Stomatitis.—It is believed that this condition is due to the virus of herpes simplex and, like herpes, its response to treatment is poor. Gentian violet may be tried as in thrush, but it is doubtful if it has any beneficial effect. Potassium chlorate, an old-fashioned remedy, given by mouth in doses of 0·12 to 0·5 g. (2 to 7½ gr.) according to age, seems to accelerate recovery in some instances. Attention to the general hygiene, the giving of adequate fluid and prevention of constipation are stressed.

Ulcerative Stomatitis (Vincent's Infection).—This is a more serious condition often following gingivitis or aphthous stomatitis. Anærobic spiro-

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Dental Caries.—It is widely held that dental caries is caused by the acids

apple, and to ensure an ample supply of vitamin D and milk. A soft brush should be used to clean the teeth, care being taken not to injure the gums. No food should be given after the evening dental toilet.

VOMITING

The treatment of vomiting depends on its cause. Mothers frequently seek

pledgets of wool to plug the nostrils or gags which prevent the mouth from

opened, have been advocated, but they rarely meet with success. Probably the best results are obtained by getting the mother or nurse to occupy the child's attention after each feeding till he falls asleep. Thickened feeds, being more difficult to regurgitate, are also helpful. Any of the farinaceous foods, such as oat flour or Sister Laura's Food, may be used for this purpose.

Hiatal Hernia.—This condition is one which is now recognized as a common cause of persistent vomiting in infants The manifestations are [illegible]

Improvement is slow. Feeds thickened with oat-flour or Farex (3 to 4 tea-spoonfuls to each feed) may help to check vomiting In intractable cases surgical treatment must be considered.

Mechanical Obstruction at the Pylorus.—This is a common cause of intractable vomiting in young infants. The obstruction may be due to spasm of the pyloric sphincter or to spasm combined with hypertrophy of the muscle (hypertrophic pyloric stenosis).

In *pylorospasm* treatment should be carried out on purely medical lines [illegible]

(Eumydrin) given in doses of 2 5 to 5 ml. of a 1 10,000 solution half an hour [illegible]

skin to become dry and there may be some rise in temperature If these symptoms become unduly pronounced, the drug should be omitted before one or two feeds or the dose reduced

Hypertrophic Pyloric Stenosis—Opinion is divided regarding the relative [illegible]

available, operative treatment is to be recommended. Although we are in favour of operative treatment in the majority of cases, there are circumstances in which [illegible] endeavouring by non-operative measures to tide him over the comparatively short period of three or four weeks when spontaneous cure will occur, rather than subject him to the risks of operation

The chief objection to medical treatment of the three- or four-weeks-old infant is that it has to be continued for many weeks, during which time the enfeebled and emaciated patient may succumb to some intercurrent disease. [illegible]

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Ulcerative Stomatitis (Vincent's Infection).—This is a more serious condition often following gingivitis or aphthous stomatitis. Anærobic spirochætes and fusiform bacilli are seen in stained smears from the lesions. Local treatment consists in cleansing the mouth with swabs dipped in hydrogen peroxide and the application of penicillin, 1,000 units per ml. four-hourly. An alternative treatment is the application of equal parts of liquor arsenicalis and tincture of ipecacuanha with an equal amount of glycerin, using a camel-hair brush. Systemic disorders and dietetic deficiencies should of course receive attention.

Dental Caries.—It is widely held that dental caries is caused by the acids produced from carbohydrate fermentation in the spaces in and around teeth, and that this is specially liable to occur in poorly calcified teeth. The indications, therefore, are to limit the consumption of sticky sweets (toffee, chocolate), to encourage a diet of hard and fibrous substances, e.g. rusk, toast, fruits such as apple, and to ensure an ample supply of vitamin D and milk. A soft brush should be used to clean the teeth, care being taken not to injure the gums. No food should be given after the evening dental toilet.

VOMITING

The treatment of vomiting depends on its cause. Mothers frequently seek advice because the baby brings up mouthfuls of milk after each feeding. In many cases this is not of serious significance, and if weight is being gained satisfactorily it may be disregarded. Sometimes, however, there is considerable loss of food and the infant does not thrive. In these cases there is probably some error in feeding technique. It may be that the child is placed flat on his back immediately after taking his feed and, in his endeavours to eructate ingested air, brings up a mouthful of food. To prevent this he should be held in the semi-erect [illegible]

correct and may lead to severe inanition. Various mechanical devices, such as pledgets of wool to plug the nostrils or gags which prevent the mouth from being

opened, have been advocated, but they rarely meet with success. Probably the best results are obtained by getting the mother or nurse to occupy the child's attention after each feeding till he falls asleep. Thickened feeds, being more difficult to regurgitate, are also helpful. Any of the farinaceous foods, such as oat flour or Sister Laura's Food, may be used for this purpose.

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given at three-hourly intervals, one feed during the night being omitted. Certain spasmolytic drugs have been used with success. Atropine methyl nitrate (Eumydrin) given in doses of 2 5 to 5 ml. of a 1 · 10,000 solution half an hour before each feed is probably the best. It may also be given sublingually as a 1 per cent. solution (0 2 to 0 6 mg) before each feed or in the form of lamellæ (Pylostropin) which can be placed under the tongue. Over-dosage causes the skin to become dry and there may be some rise in temperature. If these symptoms become unduly pronounced, the drug should be omitted before one or two feeds or the dose reduced

Hypertrophic Pyloric Stenosis—Opinion is divided regarding the relative

but failing this, and especially if the services of an experienced surgeon are available, operative treatment is to be recommended. Although we are in favour of operative treatment in the majority of cases, there are circumstances in which medical treatment should be adopted. In the presence of respiratory or gastro-intestinal infections or of skin sepsis, operation is contra-indicated, and in the child who is brought for advice when eight or nine weeks old one is justified in endeavouring by non-operative measures to tide him over the comparatively short period of three or four weeks when spontaneous cure will occur, rather than subject him to the risks of operation.

The chief objection to medical treatment of the three- or four-weeks-old infant is that it has to be continued for many weeks, during which time the enfeebled and emaciated patient may succumb to some intercurrent disease. This danger is specially to be feared in hospital practice, where isolation cannot as a rule be carried out as efficiently as in the private home.

Where surgical treatment has been decided upon, the best results are obtained

proportion of one teaspoonful for each three ounces of feed, and finally, in infants over ten weeks of age, the half-cream milk should be gradually replaced by full-cream milk and vitamin supplements added. Relapses are frequent and as a rule necessitate repetition of the régime beginning with a shorter starvation period.

Parenteral infections are of frequent occurrence, and whether one regards them as primary or secondary they should be treated by the use of sulphonamides or antibiotics. It is difficult to justify the withholding of these preparations Infants who receive one of the sulphonamides and/or an antibiotic seem to improve more quickly and relapse less frequently than those to whom none has been given. The reason for this may be found in the prevention of secondary infection, and especially is this likely to be so in the case of the infant in hospital. Sulphonamides in suspension, e g. Trisulphonamide Mixture for Infants, N.F. will be found more convenient than pills. Castor oil and such like purgatives are contra-indicated, and grey powder, the popular panacea for all infant ailments in the past, may indeed be harmful. Rectal washouts are better avoided; they disturb the infant too much and accomplish very little.

In the severe case which is sent to hospital, treatment for shock and the administration of parenteral fluid are often matters of great urgency. The infant should be placed in a warm cot and if his temperature is subnormal, heat applied by carefully protected hot-water bottles or an electric blanket. Extract of suprarenal cortex, 1 ml, may be given and repeated in four hours. As soon as possible fluid should be given intravenously by the continuous-drip method. The fluids used in various centres vary, but plasma is regarded as the best Failing that, half-strength saline with added glucose and lactate can be recommended. Once the acute phase is over, the régime as outlined for treatment in the home is adopted.

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CŒLIAC DISEASE

This condition is a chronic diarrhœal disease having its onset usually between ten months and three years There is undoubtedly a defective absorption of fat and carbohydrate and probably ... it can be accepted that some form of dieti ... ed For many years treatment with a low ... diet was the usual practice, and it still h ... ever, has indicated that gluten, contained in wheat-flour and rye-flour but not in wheat- or ...

rye-starch but not wheat-flour or rye-flour. Relapses in children on gluten free diets can be brought about by the addition of wheat- or rye-flour containing gluten.

Assuming that the diagnosis has been established and the child comes under

treatment while having diarrhœa, it is well to begin with a restricted diet of two pints of skimmed milk daily. As a rule the stools improve and the child loses the irritability and anorexia which are so disturbing to the mother. The diet should then be gradually increased to what is normal for the age, *except* that all foodstuffs containing wheat-flour are prohibited. In countries where rye is used as a food, rye-flour is subject to the same restriction.

Gluten-free wheat-flour (i e. wheat-starch) can now be purchased (Energen Foods Ltd.), but difficulty will be experienced in making a satisfactory loaf because it is the gluten in the flour which " binds " the loaf together. Various additions such as egg-white or dried-milk powders are used as substitutes, and biscuits and cakes are more easily made than loaves. In most centres the local bakery produces—or will produce if asked—gluten-free bread. Corn-flour and [illegible] addition,

[illegible] allowed :

[illegible] ed wheat,

wheat-flakes, grape-nuts, semolina, vermicelli, macaroni, ice-cream, Ryvita (or [illegible] ltine and all soups, sauces and

[illegible] akes, oat-flour porridge (small

[illegible]

suggested, trial and error has still a place One can say that whatever treatment is adopted, some dietetic restrictions are essential The use of crude liver extract and vitamin B complex which was popular a few years ago is not based on any sound principle and cannot be recommended Folic acid is only helpful in the presence of a macrocytic anæmia associated with a megaloblastic bone marrow.

Throughout the whole period of treatment, vitamin C as orange juice or ascorbic acid (50 mg) should be given daily. Vitamin D may be given as calciferol tablets (B.P.) in doses up to 700 I U. daily. Anæmia is an almost [illegible], 0 06 to 0 2 g. (1 to 3 gr) thrice daily, [illegible] ere anæmia and an infection, absorp- [illegible] be necessary to give a blood transfusion Relapses are less common than they used to be and in some cases may be due to lapses from the dietary régime

FIBROCYSTIC DISEASE OF THE PANCREAS

This is a familiar disease presenting in three different clinical forms . (1) as meconium ileus producing intestinal obstruction in the newborn ; (2) as a chronic purulent bronchitis in older infants ; and later (3) simulating cœliac disease with the passage of pale, foul-smelling stools

The treatment is unsatisfactory. When presenting in the newborn as intestinal obstruction, operation should be recommended In older infants attempts to control the respiratory tract infection by chemotherapy are indicated The pathogen is usually a staphylococcus, and penicillin by injection or inhala-

of the cot open. Steam generated in a special kettle fitted with a funnel measuring $2\frac{1}{2}$ ft. in length is allowed to flow gently into the tent. It may be medicated by adding 4 to 8 ml. (1 to 2 teaspoonfuls) of compound tincture of benzoin to the water in the kettle.

Cyanosis.—If cyanosis is present, oxygen therapy is indicated and can be given by means of a tent such as is supplied or available on hire from Oxygenaire (London). For the newborn, a small tent, using perspex, can be easily constructed. The use of a nasal catheter cannot be recommended for young children. The funnel in front of the infant's face is very wasteful of oxygen and also relatively inefficient, especially for a restless child. The oxygen is run in at a rate of about 6 litres a minute, but the concentration of oxygen in the tent should not be allowed to exceed 40 per cent.

Empyema.—In the event of empyema developing, it is best in the first instance to persist with paracentesis combined with the local use of penicillin (see p. 69). Paracentesis should be carried out at intervals as indicated by the physical signs and temperature. In infants under one year in whom the staphylococcus is usually the invading organism, treatment by aspiration of the pus is likely to yield better results than more drastic procedures. In older children with pneumococcal infections, surgical treatment is indicated if aspiration of the pus proves ineffective. In all cases attention to the general health is important. Many of these children develop severe anæmia and, as iron in the presence of such an infection is ineffective, blood transfusion may be required.

Pulmonary Fibrosis and Bronchiectasis.—Most frequently this is the sequel to a pulmonary collapse which has resulted from bronchial obstruction. When fibrous tissue has replaced the parenchyma of the lung the process is irreversible. In this sense pulmonary fibrosis is incurable, but much can be done to minimize the resulting disabilities and make the patient's life tolerable.

General hygienic measures are important, and the greatest care should be taken to prevent respiratory infections. Abundant fresh air and a country life are of advantage, especially prolonged residence in a dry climate. In the event of a flare-up of the pulmonary infection, treatment with sulphonamides and antibiotics helps to combat the acute symptoms. Foci of sepsis in the sinuses or the tonsils should be dealt with The antra are particularly liable to be affected and special attention should be paid to the examination of this part of the respiratory tract.

Two valuable methods of treatment are postural drainage and deep-breathing exercises. Every morning on rising, the patient should be placed over the side of a bed or a chair with the head hanging down and be made to cough up as much sputum as possible. If much is obtained, this procedure should be carried out twice or even three times daily Alternatively the child may be placed face downwards on a double inclined plane (Nelson bed) and kept in this position for an hour two or three times a day. In any case, it is important that the bronchi should be emptied as thoroughly as possible Following this, the [illegible] to breathe slowly and as deeply as he is able for a

nearly always a progressive one. Hence it is in the best interests of the patient that surgical treatment should be *considered*, as a matter of routine, as soon as the extent of the disease has been defined. Clinical assessment of the whole clinical problem, radiological studies, bronchoscopy and bacteriological investigation are indispensable and they should be undertaken as a joint enterprise by the physician and the thoracic surgeon. After a period of medical treatment, and when the general condition of the patient warrants it, the affected lung or part of lung is removed. The operative risk has diminished considerably in recent years, and it is now recognized that young children are even better subjects than adults; nevertheless, the cases should be carefully chosen.

CONVULSIONS

A convulsion is probably the commonest medical emergency in childhood. The care of the child during the fit is the first consideration. There is general agreement that the hot bath or mustard bath (temperature 105° F.) is worth while if only to keep the mother or nursemaid occupied. If chloroform or ether is available, the administration of one of these general anæsthetics is the surest way of producing quiescence, but by the time the doctor is on the scene the fit is usually over. Sedatives such as chloral hydrate, 0.2 to 0.3 g (3 to 5 gr.), obviously cannot be given by mouth during a convulsion, but may be administered afterwards to prevent a recurrence. Rectal administration of chloral hydrate (double the above dose) may, of course, be given, but again it would not be retained *during a seizure*, even if the procedure were practicable. Bromides are sometimes recommended, but in the present context they should be regarded as obsolete. If the fit has continued for an hour or so, the condition should be treated as status epilepticus. Paraldehyde is effective and safe, and intramuscular injection is a convenient method of administration: the dose is 0·1 ml per kg of body-weight. Alternatively, paraldehyde can be given rectally (0.5 ml. per kg. of body-weight), but in the management of this type of medical emergency in general practice it is clearly not the method of choice. Sodium phenobarbitone is also effective but more toxic: the dose is 4 mg per kg of body-weight by intramuscular injection. When the convulsion has subsided and the muscles are flaccid, lumbar puncture may be performed. This may be justifiable if there are grounds for suspecting meningitis: as a method of aborting convulsions the procedure is disappointing and not free from danger (tissue damage, broken needle, etc.)

It is important to remember that having controlled the convulsions in the first instance it is necessary to guard against their recurrence during the next few days. For this, chloral hydrate is the most useful drug, as it is rapidly eliminated and non-cumulative in its action. The dose and frequency should gradually be diminished during the succeeding three or four days.

When the child has recovered from the fit, a full review of the case must be made in order to reach a firm diagnosis and, if possible, to remove the cause. No credence should be given to the idea that sources of peripheral irritation such as teething, worms, constipation (or diarrhœa), adherent foreskin, enlarged tonsils and so forth are commonly the cause of fits. Such a suggestion may be comforting both to the physician and the parent in so far that one need never be at a loss to discover some possible source of peripheral irritation, but actual proof is lacking of their association as cause and effect. Actually convulsions

but the parents should be encouraged to persevere, as their wholehearted cooperation is indispensable. Apart from the inconvenience entailed, which is not often an objection raised by the parents, the most serious aspect of the problem is the child's loss of sleep. It is well to advise the parents never to discuss his shortcoming in his presence nor show any undue concern. Scolding and punishment are to be deprecated. Too often his anxiety not to wet the bed is his undoing, and constant reminders in the form of encouragement or the reverse from the parents or nurse only serve to keep his affliction in the forefront of his thoughts. Such children are often unduly sensitive and punishment may be a prominent factor in perpetuating the condition.

The general health must be seen to. Enlarged tonsils and adenoids may require removal. [illegible]
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value to provide some device, such as a towel tied around the waist with the knot in the back, to prevent the child from lying on his back. Drug therapy is not of much value. Some physicians claim success with ephedrine, or if there is hypersomnia, amphetamine Belladonna, however, has the widest reputation, and its use with other methods can be recommended. Commencing with 0·3 to 0·6 ml. (5 to 10 min.) of the tincture thrice daily, the dose should be increased until moderate dilatation of the pupils and dryness of the mouth indicate that the child is fully under the influence of the drug.

In intractable cases, and in mentally deficient children in whom it is impossible to obtain co-operation special methods are justified. Sphagnum moss is a valuable absorbent for urine and it also reduces the objectionable smell. A layer of moss can be spread under the child and it can also be put into muslin bags which are placed between the thighs and against the genitals at night.

CYCLICAL VOMITING

The ætiology of this condition is somewhat obscure and its diagnosis often open to criticism There are varying shades of opinion as to what constitutes the clinical picture Infection, often trivial, and emotional upset are regarded as the two most common predisposing causes. The outstanding clinical [illegible] ...ttacks of intractable vomiting [illegible] he [illegible] of [illegible] of [illegible] n

The attack begins fairly abruptly after a few hours of lassitude. Dark [illegible]ngs appear under the eyes and vomiting sets in, even water being returned. The administration of water or saline with glucose and alkali is indicated. This can be accomplished readily by giving glucose in water or saline flavoured with orange or lemon juice by mouth. Big drinks are likely to be returned, and only [illegible] at frequent intervals should be given. It may be necessary [illegible]ndance for this purpose. Although [illegible] yet with perseverance a considerable amou[illegible] be absorbed. The water and salt combat the dehydration and the glucose helps to prevent the production of ketone bodies. The best alkali to give is sodium bicarbonate. It should be

dissolved in water and given separately in sips at the rate of 1 to 2 g. (15 to 30 gr.) four-hourly. It aids in the excretion of ketone bodies and builds up the alkali reserve

In all but the most severe cases administration of fluid by mouth will suffice. But when the vomiting is intractable and the dehydration and ketosis persist, 10 per cent. glucose in saline given by rectum is of the greatest benefit. The bowel should first be washed out and then 60 to 120 ml. (2 to 4 fl. oz.) of the glucose and saline solution run in four-hourly. If the patient is markedly dehydrated and presents alarming signs of acidosis such as air-hunger and a low

and the diet can be quickly increased

Between attacks, a high carbohydrate intake is recommended, but any drastic reduction in the amount of fat allowed is not advisable Rich foods such as pastry and suet puddings should be avoided All fruit and vegetables, because of their alkaline ash, are permitted.
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use it thus as a medicine. The children often object to it and it is a constant reminder of their affliction Cream, cod-liver oil tonics and fried foods are often given in large quantities to such children in an attempt to fatten them. This is a mistake. Such substances are better avoided. Butter should be allowed in reasonable amounts and milk in the usual quantities

PINK DISEASE

(Polyneuritic Erythrœdema)

As the ætiology of pink disease is unknown, the treatment is necessarily symptomatic. The first essential is to guard the child as far as possible from intercurrent infection. He should, whenever possible, live in good surroundings in the country. Institutional treatment is definitely contra-indicated. Relief

powdered after bathing, and in some cases a soothing lotion such as the following is useful in relieving irritation .

℞ Calamine		8 g (2 dr.)
Zinc Oxide		8 g (2 dr.)
Phenol		0 6 g. (10 gr.)
Glycerin		8 ml (2 fl dr)
Lime Water	to	120 ml (4 fl. oz.)

The arms may have to be splinted to prevent scratching. When there is great irritation of the hands and feet, relief may sometimes be obtained by allowing the child from time to time to hold them in cold water. When photophobia is a prominent symptom it may be necessary to nurse the child in a darkened room

but the parents should be encouraged to persevere, as their wholehearted cooperation is indispensable. Apart from the inconvenience entailed, which is not often an objection raised by the parents, the most serious aspect of the problem is the child's loss of sleep. It is well to advise the parents never to discuss his shortcoming in his presence nor show any undue concern. Scolding and punishment are to be deprecated. Too often his anxiety not to wet the bed is his undoing, and constant reminders in the form of encouragement or the reverse from the parents or nurse only serve to keep his affliction in the forefront of his thoughts. Such children are often unduly sensitive and punishment may be a prominent factor in perpetuating the condition.

The general health must be seen to. Enlarged tonsils and adenoids may require removal. Rest must be adequate and, if possible, the child should have a rest in the middle of the day. All undue fatigue and emotional disturbance are best avoided. The bedclothes should not be too heavy, and it may be of value to provide some device, such as a towel tied around the waist with the knot in the back, to prevent the child from lying on his back. Drug therapy is not of much value. Some physicians claim success with ephedrine, or if there is hypersomnia, amphetamine Belladonna, however, has the widest reputation, and its use with other methods can be recommended. Commencing with 0·3 to 0·6 ml. (5 to 10 min.) of the tincture thrice daily, the dose should be increased until moderate dilatation of the pupils and dryness of the mouth indicate that the child is fully under the influence of the drug.

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As the ætiology of pink disease is unknown, the treatment is necessarily symptomatic The first essential is to guard the child as far as possible from intercurrent infection He should, whenever possible, live in good surroundings in the country. Institutional treatment is definitely contra-indicated. Relief from many of the distressing symptoms of the disease can to some extent be obtained by careful nursing Thus the intensely irritating sudaminous rash may be alleviated or prevented by ensuring that no flannel or woollen garments are placed next to the skin The skin should be most carefully dried and powdered after bathing, and in some cases a soothing lotion such as the following is useful in relieving irritation

℞	Calamine		8 g. (2 dr.)
	Zinc Oxide		8 g (2 dr)
	Phenol		0 6 g. (10 gr.)
	Glycerin		8 ml (2 fl dr.)
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The arms may have to be splinted to prevent scratching. When there is great irritation of the hands and feet, relief may sometimes be obtained by allowing the child from time to time to hold them in cold water. When photophobia is a prominent symptom it may be necessary to nurse the child in a darkened room

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The attack begins fairly abruptly after a few hours of lassitude. Dark rings appear under the eyes and vomiting sets in, even water being returned. The administration of water or saline with glucose and alkali is indicated. This can be accomplished readily by giving glucose in water or saline flavoured with orange or lemon juice by mouth. Big drinks are likely to be returned, and only sips from a spoon at frequent intervals should be given. It may be necessary
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S. G. GRAHAM.

THE CARE OF OLD PEOPLE

ATTITUDE OF THE DOCTOR

MEDICAL PRACTICE among old people does not differ essentially from practice among other patients. In the past, poverty played an important part in depriving the aged sick of their full share of medical attention Again, in their professional relationship with the aged most students and many young doctors fail to appreciate the scope of therapeutics in the broadest sense of the word ; and even today, practice among old people often fails to make a strong appeal. Perhaps the main reason for this is that therapeutics is here largely a matter of teaching people how to adapt themselves to the limitations imposed on their physical and mental activities by the degenerative processes of senescence , and it is inevitable that stress should be placed on the *prevention* of physical deterioration, accidents and illness Such work is certainly less spectacular than, for example, operative surgery or the radical cure of diseases caused by microbial infection. Nevertheless, a great deal can be achieved by a rational approach to the diagnosis of disabilities in old age and by planned treatment characterized by imagination and perseverance. New advances in therapeutics have simplified the treatment of many infections, but rehabilitation of the elderly and the long-term sick continues to tax the doctor's knowledge and skill It must also be constantly remembered that the aged person, when sick, often presents a double challenge to the doctor . in addition to the disabilities of senescence there may be an independent disease with a pathological basis in no way different from that occurring in younger people It is therefore imperative to make the full routine examination customary on

view, and the fullest use should be made of all the faculties that remain

THE NATURAL HISTORY OF AGING

Some knowledge of the range of the normal bodily functions in the last decades of life is obviously necessary for the physician who undertakes the care of the aged. The subject, however, has hitherto received comparatively little attention from physicians. The classic descriptions of the physical and mental changes that accompany old age have been written by laymen, among whom Shakespeare and Cicero are pre-eminent. Little is known of the physiological processes of aging. Tissue culture shows that " the individual cells and tissues of the body, in and by themselves, are potentially immortal " (Pearl) Nevertheless, the human organism passes the zenith of physical power in the third decade of life, and after that a man must be reconciled to " an age that melts in unperceived decay." Post-mortem examination of persons who

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painful feet caused by corns. In deciding on the kind of treatment needed, the numerical age of the patient is sometimes the least important guide The restoration of normal health and activity is the objective to be kept clearly in view, and the fullest use should be made of all the faculties that remain.

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limbs, and it is not appreciably affected by dietetic measures Diminished glucose tolerance is often demonstrable and glycosuria is not uncommon (2 per cent. in Anderson's series). With advancing years there is increasing insensitivity to insulin, and in the absence of ketonuria and pruritus it is rarely necessary to give insulin to old people Achlorhydria is common and may be a factor con[illegible]
usual causes [illegible]
important. " [illegible]
but recent investigations show exactly the reverse, namely, that there is on the average an increase in the water content of the tissues of old people" (Bell, Davidson and Scarborough)

MANAGEMENT OF OLD PEOPLE IN THEIR OWN HOMES

Except in special circumstances, the fewer old people who live in institutions the better for all concerned; and it is significant that more than 95 per cent. of old people live in their own homes. The importance of the family doctor's role in preventive medicine, as this bears on the management of the aged, can scarcely be exaggerated his courteous and considerate attitude to the older members of the family encourages the others to discharge their obligations with good grace Sound advice offered by relatives is often ignored by old folk until the same guidance comes from the doctor—when it is regarded as treatment and accepted without demur Thus the general practitioner can do a great deal to maintain old people's activities and hobbies and their interest in local affairs. He can foster a wider appreciation of the dignity of old age, he can strengthen self-respect in old people, and he has unrivalled opportunities to defend them against ridicule and humiliation He should emphasize to the household the importance of safeguarding the aged from infection by relatives and others suffering from the common cold. Steps should be taken to ensure that food is protected against fly-borne infections.

The doctor's chief aim should be to prevent the bedfast state, notwithstanding the timidity and even the opposition of the old person and the family Men who retire should be warned of the danger they run in abandoning [illegible]

[illegible]

"Look at the patient lying in bed What a pathetic picture he makes the blood clotting in his veins, the lime draining from his bones, the scybala stacking up in his colon, the flesh rotting from his seat, the urine leaking from his dis-

have died of old age rarely reveals any abnormality of the vital organs. It would appear that the solution of the mystery of death in old age will come from a [illegible] iemical mechanism of cellular metabolism

[illegible] n seen in old people is attributable to a reduction in the vital capacity of the lungs brought about by increasing rigidity of the thoracic cage. Contributing factors in the cardiovascular system are [illegible]

[illegible]

artery thrombosis is unusual. On the other hand, it is by no means rare to find in the last decades of life the typical signs of rheumatic valvular disease (with or without cardiac decompensation) dating from an infection some fifty years previously.

In the same study Howell noted frequent absence of the tendon reflexes, especially of the ankle-jerk; likewise vibration sense often could not be elicited at the ankle or the knee. Joint sense was only rarely affected (1 to 3 per cent.) Abnormal pupillar[illegible] group of men agec[illegible] the past few years [illegible] over sixty—a group younger than Howell's and socially more heterogeneous Anderson found that only 5 per cent. had loss of one or more tendon reflexes. There was complete loss of vibration sense at the malleoli and knees in only 2 per cent, and in a further 2 per cent. there was partial loss at these sites; but none had lost vibration sense at the elbows and wrists Again, in this series, none showed abnormal pupillary reactions that could be attributed to senescence. Nisbet's observations made on the pupillary reflex in patients over the age of eighty at Foresthall Hospital, Glasgow, showed that only 30 per cent. failed to react Anæmia, so often assumed to be common among old people, was rare. Renal function did not suffer to any great extent except as a consequence of arteriosclerosis.

In the lungs rhonchi are fairly common and may not be accompanied by pulmonary symptoms A more serious view should be taken of crepitations—which may, of course, be part of a clinical picture of pneumonia or the heralds of approaching cardiac failure. Increased pigmentation of the skin is common and is most marked in those who have lived in dirty and verminous conditions. Ecchymoses are often found on the wrists and the back of the hands: the exposed extremities may well be more liable to trauma on account of the thin, inelastic skin and the loss of subcutaneous tissue which are characteristic of advanced old age Deafness, defective vision and occasional incontinence of urine are also noted in surveys of the health of the aged. The body temperature tends to be subnormal.

Many observers have commented on the frequency of progressive decalcification of the skeleton, increasing the liability of old people to sustain fractures. The process is accelerated by prolonged rest in bed and by immobilization of

be too heavy, and tight lacing of the shoes or boots should be avoided. In this condition leather soles are recommended rather than rubber ones Nicotinic acid in doses of 50 to 100 mg. twice or thrice daily may be tried as a means of causing vasodilatation. Excessive sympathomimetic activity of smooth muscle (in blood vessels) can sometimes be reduced by means of tolazoline hydrochloride. The first dose should be 25 mg. by mouth after food, but up to 200 mg. may be given daily in divided doses In severe cases, and where the general condition of the patient warrants it, lumbar sympathectomy should be considered (pp. 620, 621) Muscular cramps, especially in calf muscles, are common in old people and are sometimes relieved by tolazoline hydrochloride (see above).

buttocks. The daily use of dusting-powder to prevent intertrigo is important especially in obese subjects and in women with pendulous breasts.

Dizziness is a fairly common and distressing symptom, especially in advanced old age It alarms the relatives no less than the patient and is often urged as a reason for transfer to hospital. Dizziness in old people appears to be the result of defective labyrinthine control The fact that it is often precipitated by sudden change of posture suggests that the underlying lesion is aggravated by cerebral ischæmia associated with progressive arterial occlusion The labyrinthine abnor

vascular disease

after stumbling h

reflexes He must learn to avoid sudden changes of posture. Severe exacerbations

this

50 m

falling. For example, the constant use of a fireguard is imperative. At the

known, but the Cawthorne-Cooksey exercises used in the management of Menière's syndrome for the improvement of labyrinthine function are worthy of trial

Unsteadiness on the legs seems to be mainly attributable to stiffness of muscles and periarticular tissues, some, however, complain rather of a feeling of muscular weakness and say that their joints feel as if they were too loose; deterioration of muscle and joint sense appears to play an important part only in a very small minority of old people (see above) Re-education exercises (p 833) are well worth while Deafness and defective vision call for thorough examination on conventional lines As remedial measures here confer untold benefits on the aged, relatives and doctors should not dismiss these disabilities as the incurable stigmata of senility without giving the matter careful consideration

The onset of mental confusion in an old person creates a problem in

tended bladder, and the spirit evaporating from his soul." Many workers in the past ten years have confirmed the accuracy of this picture. It has been [illegible]

of the legs. The limbs ultimately become fully flexed at the knees and the thighs are brought up towards the abdomen. This complication adds to the

extremes. Like

and with a little forethought this should not be difficult to arrange, even in a large and busy household. A rest, lying down, in the middle of the day is preferable to going [illegible]

difficult places. Highly polished floors, especially if they have loose rugs on them, should not be tolerated. The need for adequate lighting on stairs is often overlooked.

Attention to minor amenities pays handsome dividends: a comfortable armchair suited to the patient's particular needs; a book-rest that lies across the arms of the chair; a convenient cupboard for his exclusive use where books, papers and other personal belongings can be kept; easy access to an extra [illegible] a bedside commode and a screen, a rubber-ferruled

the three- or four-legged walking-stick;

when a radio loudspeaker would cause inconvenience to others. These are some of the special requirements of older people, but it is scarcely necessary to add that individual needs vary. Vague generalizations are reprehensible: there is a place for two or three short conferences between doctor, patient and a sensible relative who is genuinely interested. The outcome should be a concise memorandum written by the doctor, listing the items that apply to the particular patient.

[illegible] drawing the attention of t [illegible] realistic planning of new [illegible] Such matters are of [illegible] but further discussion would be out of place in this book.

are common, [illegible] attributable to the replacement of elastic tissue by fibrous tissue in the structures around the [illegible] and this is a characteristic of senescence. No special treatment is called [illegible] exercise. In old people fibrositis [illegible] ment, and is usually an indication for a short course of physiotherapy. Painful feet often result from callosities and other minor abnormalities which are amenable to treatment by the chiropodist. Peripheral vascular disease is sometimes accompanied by troublesome paræsthesiæ in the feet, and patients may complain bitterly of a burning sensation and of "pins and needles" which are most severe at night when the feet are warm in bed. Some relief may be obtained from keeping the feet exposed to the cool air. Local applications are useless, but washing the feet in tepid water before retiring and on rising in the morning is helpful. Footwear should not

hydrochloride in full doses of 0 25 g. (4 gr.) intramuscularly on the supposition that it relaxes spasm in the cerebral arteries These two forms of treatment are still *sub judice*, but they are harmless and therefore worthy of further trial. Heparin (p. 92) has been used in the hope of preventing the extension of thrombosis in the cerebral vessels However, this form of treatment is probably dangerous in these circumstances it may convert a self-limiting thrombosis into a fatal cerebral hæmorrhage.

Old people are usually very sensitive to colds and draughts, and this is explained partly by their relative inactivity and partly because of the alterations in their cutaneous vasomotor responses. Adequate and suitable clothing is [illegible]

often find it too warm to sit in the sun.

The dietetic habits of old people vary widely. In institutions they often eat voraciously—perhaps because they have little else to interest them—but in general they eat sparingly Lack of outdoor exercise contributes to this. Another factor in many instances is the reluctance of the old, in their own homes, to go to the necessary trouble to obtain varied and well-cooked meals, thus [illegible]

chances of survival among those who have hard work to do On the other hand, if women lapse into a vegetative existence as their domestic responsibilities diminish, they are likely to become obese—especially if they fall into the common habit of eating large amounts of bread and butter, jam and cakes. Most old people are well advised to make breakfast and a midday dinner their main meals. They usually sleep better at night if they go to bed after a light carbohydrate meal In the daily dietary it is important to maintain a high intake of protein in the form of meat, fish or eggs and to eat fats sparingly, but for some old people lack of money may make this advice difficult to follow. Tea and [illegible]

differential diagnosis. No doubt the commonest cause is senile dementia consequent upon cerebral arteriosclerosis and anoxia. This diagnosis should not be made, however, before other possible causes have been excluded—incipient uræmia or the toxæmia of undiagnosed infection such as pneumonia or a deep-seated abscess. Nisbet has noticed that mental confusion may occur in old people when they experience the physical discomfort of a distended bladder, and that this precedes any rise in blood urea. The imminence of cerebral thrombosis is another possible cause. The unskilful use of drugs is a fairly common cause of mental confusion in old people. Hyoscine, bromides and barbiturates are best avoided, as they are more likely to aggravate than to relieve the symptoms. If hypnotics must be used, paraldehyde or chloral hydrate are to be preferred. Cardiac failure, usually associated with hypertension or with progressive occlusion of the coronary arteries, is a common cause of restlessness and persistent attempts to get out of bed. Not every patient who is apparently restless is abnormal; an old person may be convinced with good reason that he should visit the bathroom. A patient's behaviour when overtaken by cerebral softening probably reflects somewhat on the skill of the physician and nurses who have cared for him. Excessively rigorous suppression of the restless patient is often followed by violent resistance. In these matters judgment and experience count greatly, but the Shakespearian injunction is worth remembering:

> Fetter strong madness in a silken thread,
> Charm ache with air, and agony with words.

... distressing to those who tend the
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rmined,
yncope,
Cosin
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adness.
The intravenous injection of about 50 ml. of 50 per cent. glucose solution is
... The use of digitalis,
It need only be added
pisodes of congestive
hould therefore watch
his patient closely and be prepared to stop treatment *early* if it fails, rather than expose the patient to the additional hazards of poisoning.

Patients who develop cerebral vascular catastrophes (other than minor lesions with fleeting symptoms) should be admitted to hospital as medical emergencies. They require continuous expert nursing and orthopædic management to prevent overstretching and damage to paralysed muscles; and the first phase of physiotherapy should be started at once (p. 833). The hygiene and feeding of the helpless patient, who is often unconscious and incontinent, can rarely be undertaken satisfactorily in a private house. Failure to admit such
... diminishes

malignant disease; and ill-health arising from *defective personal hygiene* and *faulty nutrition*. The immediate treatment of all these conditions will be found in the appropriate sections of this book. Certain problems, however, call for special comment:

Incontinence.—For obvious reasons the onset of incontinence provides an absolute indication for transferring a patient from his home to hospital. As already stated, when a patient is allowed to become bedridden, incontinence almost invariably follows sooner or later. A high proportion of patients who have developed this complication recover normal control of the sphincters when they have been taught to walk again The importance of this observation in relation to the prevention and treatment of incontinence does not need to be laboured. Wilson has shown that frequency and precipitancy of micturition is often associated with over-activity of the neuromuscular mechanism of the bladder In these cases the bladder function may improve by using the cystometer to bring about gradual distention and by inhibitory re-educative training. Soiling of the skin with urine and fæces necessitates prompt and frequent attention from the nursing staff, not only for the immediate comfort of the patient but also to prevent maceration of the skin, infection and the development of pressure sores

There are many patients classed as incontinent of fæces who have not in fact lost control of the sphincter but who have become unable to empty the rectum completely unless they are allowed a long time. Accordingly it is recommended that these patients should devote an hour or so every day to the task of emptying the lower bowel completely They should be provided with a bedside commode and a screen, care being taken to ensure comfort and warmth, and the patient should be encouraged to read and smoke if he so desires. The use of purgatives merely complicates the management of these cases, but a simple enema twice or thrice weekly may be necessary as a preliminary to the use of the commode. Much can be done to prevent the inconvenience of incontinence by instituting in the ward a two-hourly round of urinals and bedpans. The disadvantages of the bedpan and the bedside commode can be avoided by using the Bohmanson chair—essentially a W.C seat fitted into a wheel-chair The patient is thus transported to the bathroom and, remaining seated in the chair, is placed in position over the W.C. For a limited number of incontinent and permanently bedridden female patients a special bed designed to permit of simple drainage of excreta has been used successfully (Brocklehurst, 1950) It should be tried only when other methods of treatment have proved unsatisfactory Patients must not be restless but must lie still in the dorsal position in the moulded bed; those with contracture deformities of the lower extremities are excluded from this method of nursing

A troublesome development among many incontinent patients is their habit of contaminating their hands with their excreta Many of these offenders are rational and behave well in other ways, but show great resourcefulness in pursuing this extremely unpleasant practice A method of nursing which has been found useful in dealing with this problem has been published by Arnott (1952)

Hemiplegia.—The general principles of treatment consist in preventing damage to paralysed muscles and maintaining the functional efficiency of all joints Practical details should be obtained from manuals of orthopædics and physiotherapy. The procedures are outlined below:

and the irritation set up causes the patient to pass frequent liquid motions. It is usually necessary to remove these masses digitally after lubrication with liquid paraffin. Thereafter, neostigmine, 15 mg. by mouth, four times daily after meals for a few days is useful in preventing recurrence: this type of constipation scarcely warrants the use of irritant purgatives.

The onset of actual illness is a signal for immediate investigation and treatment. One of the hazards to which the aged are exposed is the practice among the laity to attribute all ill-health to the patient's advanced age and to defer seeking medical help. Old people are, of course, susceptible to most of the diseases that afflict those of middle age, such as pneumonia, cholecystitis, hypertensive heart failure, infection of the urinary tract, arthritis, etc., and appropriate treatment for such conditions is described elsewhere in this book. The early use of antibiotics, e.g. penicillin, in the first few hours of respiratory tract infections is often valuable, even though it may only prevent the spread of *secondary invaders.*

MANAGEMENT OF OLD PEOPLE IN HOSPITAL

patients who

community.

and administ

numbers of aged infirm people. It is generally agreed that the medical care of old people should fall within the scope of every practitioner; but it must also

The hospital physician who is responsible for the care of a large number of aged and infirm folk will find it profitable to classify them into fairly homogeneous groups. It is desirable to have wards reserved for new admissions where diagnostic work and careful assessments can be made prior to prescribing

mentally normal

There are few indications for modifying the general management of a patient in hospital merely on the grounds of old age. If the doctor's approach to diagnosis and treatment is the same as that adopted for patients in younger age-groups, he will seldom be far wrong in his handling of the case. The diseases and disabilities most commonly encountered among the aged in hospital are: *degenerative diseases of the cardiovascular system* resulting in cardiac insufficiency, cerebral vascular catastrophes with paralysis, progressive arteriosclerotic dementia, and senile gangrene; *arthritis of various kinds*,

important to seize every opportunity to apply advances in medicine, in hygiene and in other fields to the welfare of the aged. The use of deodorants in wards occupied by incontinent patients is one example; and in suitable cases the charcoal blanket is a boon not only to the patient but indirectly to patients in [illegible] old-fashioned sputum mug should be [illegible] such receptacles is an unnecessary [illegible] de of waxed cardboard and provided [illegible] n be collected by an orderly several times daily and destroyed in the incinerator Methods and appliances in the ward kitchen and in the sanitary annexes should be reviewed by the physician from time to time.

S. Alstead.

1. The use of the Balkan beam or the Guthrie-Smith frame to permit of *suspension and extension of* the affected limbs.
2. The immediate institution of *passive movement*, all joints being put through a full range of movement twice daily.
3. The encouragement of *active movement* as recovery occurs, and the maintenance of power in all other muscles of locomotion, including those of the trunk.
4. Transfer of the patient from bed to a chair for treatment as soon as it is feasible.
5. Stimulation of active movement, especially of the extensor muscles, by faradism twice daily over a period of several weeks.
6. The use of exercises designed to teach the patient to raise himself from
7. ... es in walking, first with human ... ids and finally without help of any kind

Contracture Deformities.—Contracture deformity is one of the complications of the bedfast state. The patient who is kept in bed for months or years usually becomes apathetic and morose. In this state he spends an increasing proportion of his time curled up, assuming a posture recalling that of the fœtus *in utero*. Even in the absence of organic disease of the locomotor or nervous systems, such patients are liable to develop contractures by spontaneous shortening of muscles and tendons. The only rational approach to this problem is preventive: the bedfast state must be avoided at all costs. Remedial surgical and orthopædic measures are of limited value. It is a relatively simple matter ... ent is still left with ... of contractures, the ... contractures of the knees may be corrected simply by suspending the limbs by the ankles in a *Guthrie-Smith frame. Surprising success has often been achieved in this way.* The difficulties of the surgical approach to these cases are, of course, greatly increased if ankylosis has occurred in any of the joints of the contracted legs.

It must be admitted that even with the most enlightened management of patients with paralysis, arthritis and other locomotory disabilities, it is likely that a time will come when attempts to walk or to use a wheel-chair must be abandoned. Such patients *have reached the bedfast state and are liable to* develop contracture deformities. The onset of these disabilities can, however, be delayed by continuing physiotherapy; active and passive movement of the joints should still be carried out, and massage *often prevents and relieves* painful muscle spasm.

WARD HYGIENE AND GENERAL WELFARE OF OLD PEOPLE IN HOSPITAL

Careful attention to every aspect of ward hygiene is particularly important when the great majority of the patients are long-term cases High *standards*

staff, the ultimate responsibility is the doctor's, and he can help ... colleagues by showing a practical interest in their work and their problems. It is

charcoal blanket is a boon not only to the patient but indirectly to patients in neighbouring beds (Alstead, 1942) The old-fashioned sputum mug should be banished, if only because the washing of such receptacles is an unnecessary imposition on the nursing staff Cups made of waxed cardboard and provided with lids should be substituted, they can be collected by an orderly several times daily and destroyed in the incinerator Methods and appliances in the ward kitchen and in the sanitary annexes should be reviewed by the physician from time to time.

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to straighten limbs and perform arthrodesis; *but the patient is still left with* severely wasted muscles In the orthopædic management of contractures, the effect of gravity should be fully exploited. For example, contractures of the knees may be corrected simply by suspending the limbs by the ankles in a Guthrie-Smith frame. Surprising success has often been achieved in this way. The difficulties of the surgical approach to these cases are, of course, greatly increased if ankylosis has occurred in any of the joints of the contracted legs

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laxis of compressed air illness almost since the time of recognition of the properties of helium. In the treatment of tubal and sinus block and æro-otitis the nose is sprayed with a 2 per cent. solution of ephedrine sulphate preparatory

a pressure of 12 mm of mercury Obstinate cases may require ten minutes, longer treatment is useless. It has been found that treatment with helium reduces the number of days lost from work and decreases the incidence of suppurative otitis media

WORK WITH PNEUMATIC DRILLS

The tissue changes and vasomotor disturbances that develop in the hands are not amenable to treatment This industrial disease would rarely be seen if employees were prohibited from working with pneumatic drills for more than one year.

MINER'S NYSTAGMUS

The overwhelming importance of *prevention*, the danger of taking too limited a view of the patient's needs, and the lack of a specific cure—all these points emerge in the following brief extracts from official reports:

"Although it is of fundamental importance that every effort should be made to improve the lighting of mines yet it is also of the utmost importance

POISONING BY METALS

Lead.—Lead is a cumulative poison. Small quantities are absorbed over a long period of time, and the toxic effects nearly always appear in a chronic form The risks are obvious in such occupations as lead-mining and lead-smelting Lead is widely used in industry and there are many occupations which carry some risk of plumbism · it is needed for electric batteries and in cable coverings, type metal and brass alloys; and a number of manufactured goods such as paint, rubber and glazed pottery contain lead In Britain cases of lead poisoning still occur as a result of inhalation of lead vapour in the course of ship-breaking by the use of oxy-acetylene. In this occupation preventive

[1] Reports of the Miners' Nystagmus Committee of the Medical Research Council, 1922 and 1932

[2] Report of British Medical Association to Departmental Committee

The drink can be made more palatable by modification thus:

Sodium chloride	0·45 kg. (1 lb.)
Potassium chloride	0·33 kg. (10½ oz.)
Citric acid	0·17 kg. (5½ oz.)
Saccharin	3 g. (45 gr.)
Oil of lemon	25 ml (6·2 fl. dr.)
"Lemon squash" colouring . .	q s.
Water . . .	to 3 litres (5·28 pints)

Add 1 part of this concentrated solution to 30 parts of water.

Tablets containing similar ingredients are now available for the ready preparations of palatable saline drinks

WORK IN UNUSUAL ATMOSPHERIC PRESSURES

Compressed Air.—Another type of strain on physiological adaptation is that involved by work in compressed air. Among the precautions taken to prevent compressed air illness are (1) medical supervision by physicians with experience of work entailing the use of compressed air; (2) preliminary medical examination of personnel; (3) limitation of hours of work in compressed air, (4) *slow decompression, with rigid adherence to a prescribed technique*; and (5) provision of a hospital lock for dealing with cases of caisson sickness. In selecting workmen the essentials are normal lungs, normal kidneys, and a good heart; blood pressure should not be above normal. According to Singstad, many American States have codes of regulations which require supervision by a qualified physician experienced in work with compressed air to secure (*a*) examination of each new worker, (*b*) test of each new man under actual working conditions; (*c*) re-examination of any man absent from work for ten days or more, (*d*) periodic re-examination of all workers; (*e*) prohibition of employment of alcoholics; (*f*) complete record of all examinations and illnesses; (*g*) a medical lock 5 to 6 ft in diameter, with a physician in constant attendance when pressures exceed 17 lb per sq. in. Adequate dressing-room facilities should be provided and hot coffee should be served to workers on their return from the air chamber.

In Britain the *Committee on Regulations for Work carried out in Compressed Air* recommended that after 25 to 40 lb. pressure men should be kept for forty minutes after decompression before leaving the works, and that with 40 to 50 lb. pressure they should be kept for one hour.

Recompression and slow decompression is the recognized treatment of compressed air illness. It should be used as soon as possible after the onset of the illness The American Naval Medical Research Institute has reported great success from the use of a standard technique which includes three basic principles: (*a*) limitation of recompression to a maximal pressure of 65 lb. per sq. in., maintained for from 30 to 120 minutes, (*b*) more prolonged recompression for periods of 12 to 24 hours at pressures equal to depths between 30 and 60 ft.; and (*c*) inhalation of oxygen to promote more rapid elimination of nitrogen

Helium oxygen mixtures have been suggested for the treatment and prophy-

lost in giving a tablespoonful of Epsom Salts in half a tumbler of warm water followed by two cups of hot tea Meanwhile, if colic recurs or is not completely relieved, a hot-water bottle should be applied to the abdomen through a single layer of blanket. If this fails to abolish pain, spasmolytics may be tried Hyoscine hydrobromide, 0·4 mg. ($\frac{1}{150}$ gr.), is the best preparation of the atropine group: the dose should be injected intravenously and the effect noted after about fifteen minutes Amyl nitrite may also be used, but the benefit is likely to be fleeting and its side-effects on the cardiovascular system are often disagreeable; a nitroglycerin tablet chewed slowly every half-hour is preferable if it suffices to relieve the colic Occasionally it may be necessary to resort to morphine, methadone or pethidine. If, however, there are exacerbations of symptoms over a period of weeks, the use of these analgesics is obviously not without risk of producing addiction Saturnine encephalopathy calls for the use of barbiturates such as pentobarbitone, 0·3 g ; and if treatment makes the patient drowsy or unconscious, the appropriate nursing care will be needed; and in particular it will be necessary to record fluid intake and output.

Splinting, massage and electricity (notable galvanism) have been found useful measures in the management of lead paralysis

Definitive Treatment.—It is convenient to consider here those therapeutic measures which can be explained on the basis of what is known of the metabolism

lead into the blood, and an exacerbation of plumbism is likely to occur. *Per contra*, an alkalotic state tends to fix the lead more firmly in the bones. It follows that measures which prevent or correct the state of acidosis are also effective in preventing or relieving lead poisoning In practice the immobilization of circulating lead is achieved by giving suitable calcium salts in large doses. A teaspoonful of calcium gluconate (about 4 g.) can be given thrice daily by mouth or 10 ml of a 10 per cent solution can be injected intramuscularly daily. At the same time the diet should be supplemented by foods rich in available calcium: milk (3 pints daily) is very effective. These measures give dramatic relief from the symptoms of acute plumbism.

De-leading.—The controlled shifting of accumulated lead from the bones in order to facilitate its excretion from the body would appear to be desirable on general grounds. The process is called " de-leading the patient " The most favoured method consists in depleting the body calcium by means of the acid-forming salt ammonium chloride—which tends to produce acidosis Alter-

increases the excretion of lead, but as its action is fleeting and erratic, the use of parathyroid is no longer recommended If de-leading is attempted, it should normally be undertaken only in hospital and after acute symptoms of plumbism have completely subsided. The promotion of mild acidosis is accelerated by giving a low calcium diet, that is by restricting the quantity of milk, cheese, egg-yolk and green vegetables. Notwithstanding the theoretical attractiveness of de-leading techniques, it must be emphasized that lead which remains in the bones is entirely harmless. Authority is not lacking for the view

measures are difficult to apply and the clinical picture is more acute than that usually seen in other forms of industrial lead poisoning. Much time and energy have been spent in devising methods to prevent plumbism among workmen, and a great deal has been achieved. The number of cases now reported annually does not exceed 100—with a death-rate of about 10 per cent. At the same time this statement certainly does not reflect a complete picture of industrial plumbism. To quote Dreisbach (1955): "Most of these cases of lead poisoning have been discovered in a few hospitals, and it is possible that the incidence of

must be admitted that however ingenious and effective the devices may be for the prevention of industrial poisoning, their value in practice depends on the

form of fuel It is noteworthy that children are particularly susceptible and the mortality in young people is high.

Periodic clinical examination has proved to be of little value in anticipating the onset of symptoms, but it has been shown that systematic examination of blood films (at intervals of not less than one week) in conjunction with clinical examination can be of real assistance. Inhalation of lead-fume rapidly produces characteristic changes in both white and red blood cells, the latter mainly in the form of punctate basophilia. *It is important to realize that punctate basophilia is not a sign of poisoning:* it is a finding which is consistent with the absorption of potentially harmful quantities of the metal. So long as the hæmopoietic tissues can respond briskly in this way to the presence of lead, there does not appear to be imminent danger of collapse *In brief, the existence* of plumbism is confirmed by the discovery of excessive quantities of lead in the

... of plumbism are described below.
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Skilfully ... has
relief ...
significant quantities of lead stored in his tissues and who is accordingly liable to exacerbations of poisoning. Our therapeutic measures have important limitations and these serve to emphasize that *the preventive aspects of lead poisoning are still by far the most important.*

Symptomatic Treatment.—If the management of a patient suffering from plumbism is to be adequate, careful study of all the circumstances will be required. The patient's *immediate* needs must, however, receive attention. The most reliable method for relieving lead colic is to inject slowly intravenously a soluble calci ... The
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layer of blanket. If this fails to abolish pain, spasmolytics may be tried. Hyoscine hydrobromide, 0 4 mg. ($\frac{1}{150}$ gr.), is the best preparation of the atropine group: the dose should be injected intravenously and the effect noted after about fifteen minutes. Amyl nitrite may also be used, but the benefit is likely to be fleeting and its side-effects on the cardiovascular system are often disagreeable; a nitroglycerin tablet chewed slowly every half-hour is preferable if it suffices to relieve the colic. Occasionally it may be necessary to resort to morphine, methadone or pethidine. If, however, there are exacerbations of symptoms over a period of weeks, the use of these analgesics is obviously not without risk of producing addiction. Saturnine encephalopathy calls for the use of barbiturates such as pentobarbitone, 0 3 g.; and if treatment makes the patient drowsy or unconscious, the appropriate nursing care will be needed; and in particular it will be necessary to record fluid intake and output.

Splinting, massage and electricity (notable galvanism) have been found useful measures in the management of lead paralysis.

Definitive Treatment.—It is convenient to consider here those therapeutic measures which can be explained on the basis of what is known of the metabolism of lead. In the body lead is stored in the bones and poisoning does not occur so long as it is thus immobilized However, should systemic acidosis develop, the call upon the fixed base of the body results simultaneously in a flow of lead into the blood, and an exacerbation of plumbism is likely to occur. *Per contra*, an alkalotic state tends to fix the lead more firmly in the bones It follows that measures which prevent or correct the state of acidosis are also effective in preventing or relieving lead poisoning In practice the immobilization of circulating lead is achieved by giving suitable calcium salts in large doses A teaspoonful of calcium gluconate (about 4 g.) can be given thrice daily by mouth or 10 ml of a 10 per cent. solution can be injected intramuscularly daily. At the same time the diet should be supplemented by foods rich in available calcium: milk (3 pints daily) is very effective. These measures give dramatic relief from the symptoms of acute plumbism.

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favoured method consists in depleting the body calcium by means of the acid-forming salt ammonium chloride—which tends to produce acidosis Alter-

[illegible]

increases the excretion of lead, but as its action is fleeting and erratic, the use of parathyroid is no longer recommended If de-leading is attempted, it should normally be undertaken only in hospital and after acute symptoms of plumbism have completely subsided The promotion of mild acidosis is accelerated by giving a low calcium diet, that is by restricting the quantity of milk, cheese, egg-yolk and green vegetables. Notwithstanding the theoretical attractiveness of de-leading techniques, it must be emphasized that lead which remains in the bones is entirely harmless. Authority is not lacking for the view

that in these circumstances there is much to be said for leaving well alone: the risk of recurring plumbism can be virtually eliminated by ensuring that the diet is rich in calcium. This conservative attitude towards the management of plumbism is all the more acceptable now that chelating agents have been found to be so valuable in dealing with exacerbations of lead poisoning.

Chelating Agents (Gk. *chele*—claw) —The introduction of these substances represents perhaps the most important advance in the therapeutics of lead poisoning. The preparations in common use are edetic acid (Edathamil, ethylene diamine tetra-acetic acid) and the calcium compound calcium disodium ethylene diamine tetra-acetate (Versenate, Sequestrine). Lead is one of the metals for which Versenate has a great affinity—so much so that the lead ... *is formed a new* ... -toxic substance

Preparations of edetic acid are non-toxic when administered therapeutically. they may cause a temporary fall of blood pressure, but this is not important. Calcium disodium edetic acid combines with certain other metals—iron, copper and magnesium Care must therefore be taken that its use does not *result in depletion of metallic ions which are essential for normal metabolism,* and prolonged courses of treatment are therefore to be avoided. Calcium disodium edetic acid is put up in 20 per cent. solution in 5 ml (1 g.) ampoules (Riker Laboratories). The dose is 1 g. per 20 kg. body-weight administered intravenously in 100 ml. 5 per cent. dextrose solution over a period of two hours ... A course of treatment lasts up to five days, and a similar

... *in lead poisoning has been* abandoned. In plumbism the administration of dimercaprol produces interesting pharmacological effects · within a few minutes there is a sharp fall in the levels of lead in the blood, showing a shift of the metal into other body tissues, but there is no important increase in the amount of lead excreted.

Arsenic.—Cases of poisoning by arsenical salts are nowadays rarely seen in industry. The general preventive measures that have been found most useful are substantially *the same as those for the prevention of lead poisoning.* ... The prevention of poisoning by arseniu- ...

in closed apparatus or under good artificial exhaust ventilation. ... mercury bromide paper, which show by a yellow colour small traces of arseniuretted hydrogen, *should be hung in the workrooms.* In the face of a known ... regular

... a-

tion of a large proportion of the hæmoglobin—for which arsine has a special affinity. The first essential is the administration of oxygen. Transfer to hospital should then be arranged. It should be assumed that blood transfusion will be needed (*see p. 861*). Dimercaprol is of no value in the treatment of arsine poisoning, but good results are obtained from dimercaptopropyl ethyl ether. Convalescence is always slow. several months may elapse before the patient has regained normal health.

The treatment of *chronic arsenical poisoning* consists in removal from exposure and in promoting elimination through kidneys and bowels

In the treatment of arsenical poisoning dimercaprol (BAL) is invaluable.
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ago The recommendations of Thackrah (1833) are still valid—personal cleanliness, change of dress and attention to ventilation

It is important to secure limitation of the area of mercury exposed to the air. The workroom should be kept cool, since volatilization increases rapidly with temperature Floors and work-benches should be smooth and impervious and should drain to a collecting trough All vessels containing mercury should be kept covered.

Frequent attention to the teeth is desirable: they should be examined regularly and necessary dental treatment undertaken; regular brushing is important, and the use of a mouth-wash:

Alum	0 3 g (5 gr)
Potassium chlorate	0 3 g. (5 gr.)
Glycerin	2 ml. (½ fl. dr.)
Water	to 30 ml. (1 fl. oz)

For the prevention of ulcers from exposure to fulminate of mercury the use of a 10 per cent. solution of sodium hyposulphite is recommended as a local application.

In the selection of workers, women and young persons should be excluded It is particularly important to reject applicants found to be suffering from renal or pulmonary disease.

The actual treatment of chronic mercurial poisoning consists largely in removing the patient from exposure to mercury, in attention to his general [illegible]

belladonna, e g. dry extract of belladonna, B P., 30 mg (½ gr) twice or thrice [illegible]

cent. solution of sodium hyposulphite is used as an eyewash.

Selenium.—Selenium is being increasingly used in industry· it affects chiefly the liver (with atrophy and cellular destruction mainly around the central vein), kidney, blood (with primary increase in hæmoglobin followed by distinct decrease) and the skin

Prevention follows lines already described, in addition, the wearing of a simple gauze mask has been found useful in preventing the collection of dust in

upper nasal passages (catarrh; epistaxis) All operatives with symptoms, however vague, should be carefully examined, with hæmoglobin estimation and a test for urinary selenium in a twenty-four hours' specimen The administration of 0·2 ml. (3 min) of bromobenzene three times a day after meals for short periods not exceeding five days causes selenium fixed in the tissues to appear in the urine.

Beryllium.—The *symptoms following* exposure to beryllium have been reported mainly among workers in fluorescent-lamp factories; they include

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mortality (10 per cent. compared with 2 per cent. in pulmonary granulomatosis of chronic beryllium poisoning) The first symptoms of chronic disease may not appear for some years after exposure to beryllium. Weakness, anorexia and progressive loss of weight occur early, then a persistent dry cough, and finally severe *dyspnœa. Radiological changes take the form of fine nodulation*, but the skiagram is not diagnostic.

In acute and chronic pulmonary berylliosis the indications for treatment are determined by the state of oxygen deficiency (p. 880), the presence of asthma (p. 683) and by signs of right-sided heart failure (p. 519). Cortisone should

DIMERCAPROL (BRITISH ANTI-LEWISITE) IN THE TREATMENT OF POISONING BY SOME HEAVY METALS

This compound, 2, 3-dimercaptopropanol, was developed during the Second World War as an antidote to arsenical gases such as Lewisite Fortunately it

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ference with the sulphydryl enzyme systems of cell proteins. It follows that any substance which "offers" a large number of sulphydryl groups is potentially of therapeutic value: if it can diffuse into the body tissues it may *satisfy the* affinity of a heavy metal for sulphydryl and thus safeguard this grouping in certain enzymes which are indispensable for normal metabolism Early research showed that one molecule of an arsenical combined with two SH groups. From this observation is was accurately *predicted that the dithiols of the dimercaprol* type would be more powerful antidotes than the monothiols. The history of these compounds ranging from Ehrlich's fundamental observation in 1909 to the war-time investigations of Peters and his colleagues (published in 1945) have a secure place in classic medical research

Sulphydryl enzyme systems are inhibited not only by arsenic but also by mercury, bismuth and cadmium in very low concentration—something of the order of $10^{-5}M$. Lead and vanadium have the same effect but at higher concentrations ($10^{-4}M$); relatively high concentrations of zinc and antimony are needed—which means that the toxic effects of these metals are less easily combated by *the dithiols The complex formed* by the interaction of a heavy metal and a dithiol is relatively stable and in this form it may be excreted without

harm. There is, however, some tendency to dissociation and a risk of recurring toxæmia It is therefore important to ensure that the dithiol available is always somewhat in excess of immediate requirements this is achieved by adequate dosage and repeated administration.

Dimercaprol is administered by intramuscular injection as a 5 per cent. solution in arachis oil with benzyl benzoate. Skin lesions are no longer treated by inunction, but contamination of the eyes with arsenical vesicants can be treated with a 5 per cent oily solution instilled into the conjunctival sac; complete recovery follows prompt treatment. With the exception of aplastic anæmia, all the toxic effects of severe arsenical poisoning can be relieved, but success depends largely on *early treatment* and especially on giving adequate doses in the first forty-eight hours The following dose schedules incorporate recommendations set out in the BPC 1954 for the treatment of arsenical poisoning with dimercaprol.

Day	(*a*) *Severe Poisoning* Dose 3 mg /kg body-weight	(*b*) *Mild Poisoning* Dose 2·5 mg /kg. body-weight.
First	6 doses	6 doses
Second	6 ,,	6 ,,
Third	4 ,,	2 ,,
Fourth-Tenth	2 ,, daily	1 or 2 doses daily

[illegible]

POISONOUS FUMES, GASES AND ORGANIC SOLVENTS

[illegible] diseases.

Carbon Monoxide.—The immediate treatment of carbon monoxide poisoning is directed to (1) restoration of normal breathing, and (2) abatement of shock. Immediately the patient has been carried into the fresh air, artificial respiration should be applied It is important that the patient be kept warm by the use of blankets and hot-water bottles while treatment is being carried out. At the start the general management of the patient is that adopted for the unconscious patient. Sudden death in the early stages of recovery is not unusual after severe poisoning: it is wise therefore to give a guarded prognosis Arrangements are immediately put in hand for the administration of *pure oxygen* (p. 880) Formerly oxygen containing 7 per cent carbon dioxide was

given, but this has been abandoned; the tissues of the anoxic patient contain more than enough CO_2 to stimulate the respiratory centre, and adding more by inhalation produces a serious risk of carbon dioxide intoxication. The inhalation of oxygen should be continued for at least twenty minutes after the restoration of spontaneous respiration.

Blood transfusion has been recommended, but it is useless unless performed within an hour of the patient's removal from the gas-laden atmosphere. The spontaneous elimination of carbon monoxide by the end of one hour renders transfusion unnecessary: the patient is by that time suffering from the late effects of asphyxia, which are not relieved by transfusion. German observers report that massive venesection is often of value in these cases.

Respiratory stimulants such as aminophylline and lobeline have been tried but are rarely of any value. Even if the respiratory centre is susceptible to their action, the effect is too transient to be of therapeutic importance. Methylene blue was formerly used in the hope that it would function as a substitute for tissue oxidases inactivated by CO poisoning. Further examination of this method of treatment shows it to be irrational and dangerous. In short, effective treatment depends on efficient oxygen therapy: at present we have no drugs which are of any value in CO poisoning.

If manometric readings show that the headache is associated with increased intracranial pressure, 20 ml of 50 per cent. dextrose should be injected slowly intravenously. Aspirin may be used as an analgesic for headache, but drugs of the phenacetin series should be avoided because of their tendency to immobilize hæmoglobin as methæmoglobin.

A person who has been gassed should not be allowed to walk home: transport must be provided. He must be ordered to remain in bed for a few days after all symptoms have disappeared, the duration of rest in bed will depend on the severity of the intoxication. The patient should have a week of gentle exercise before returning to work.

Cyanogen Compounds.—Hydrocyanic acid should be used only wit[h] meticulous care. For many years it has had an extensive vogue in the disinfestation of ships and premises, and accidents have occurred from failure to adhere to the rigid instructions laid down for effective clearing of the atmosphere before re-entry.

Many cases of cyanide poisoning will inevitably be fatal. death occurs once from large doses, and even after small quantities much depends on th speed with which specific treatment is made available. Cyanide prevent ellular metabolism dependent upon cytochrome oxidase. The complex which s formed with the oxidizing enzyme, however, is dissociable: thiocyanate is ormed in the tissues and enzyme activity is restored. Immobilization of cyto- rome oxidase can be prevented by "offering" methæmoglobin to the cyanide n. Cyanmethæmoglobin is thus formed and then sodium thiosulphate is ven to combine with cyanide released from the cyanmethæmoglobin and fix s thiocyanate. The formation of methæmoglobin in the patient's circulating od is achieved by slowly injecting sodium nitrite intravenously solved in 10 ml. water. When workmen oning this preparation er in attendance. nitrite should b minutes. Withir

...nishing the administration of sodium ... one capsule every

nitrite, the injection of sodium thiosulphate should be started, 50 ml. of 10 per cent. solution—taking about fifteen minutes to complete the treatment. As an alternative to nitrite treatment methylene blue can be used, 5 to 50 ml. of a 1 per cent. solution by slow intravenous injection, but it is much less reliable. After-care is the same as for carbon monoxide poisoning.

Nitrogen Dioxide ("Nitrous Fumes").—When symptoms of poisoning

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oxygen.

Much of the danger of these nitrous gases lies in the fact that there is often a lag of several hours between exposure to them and the appearance of acute

as serious at the time—if followed *after a few hours* by cough, expectoration, a *sense of constriction and signs of distress, point strongly to nitrogen dioxide* poisoning. Drugs make little impression on this condition, but if pulmonary œdema develops atropine sulphate (1 mg. intravenously) may be tried: although it cannot affect the volume of transudate in the alveoli, it reduces the total volume of fluid in the respiratory tract by blocking secreto-motor activity in the bronchi. When mucus accumulates in the upper respiratory tract it may be removed by means of a rubber tube attached to a mechanical sucker. If cyanosis is present, oxygen should be given (p. 880). Signs of overloading of the right-heart call for venesection. Absolute rest and careful nursing are essential.

Chlorine.—Chlorine is a typical irritant gas and its inhalation is apt to produce generalized inflammation throughout the respiratory tract.

The general principles of treatment are similar to those mentioned above (see Nitrogen Dioxide). Complete rest, oxygen therapy, treatment of shock and symptomatic measures to combat the troublesome cough are the chief measures;

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also depress the respiratory centre. Methadone, 1 to 2 mg. as a linctus, is to be preferred to morphine.

huretted hydrogen

tment of poisoning

The treatment of acute poisoning by sulphuretted hydrogen consists in artificial respiration combined, where necessary, with the inhalation of oxygen. General symptomatic treatment and after-care are as for other poisonous gases. For the irritation of mucous membranes which the gas is apt to produce when present in com-

supervene after a few hours in patients who do not at first appear to be seriously affected. On this account the patient must be closely watched for twenty-four

an exceptional case, and apart from the child diabetic, the surgical diabetic and the diabetic complicated by infection, this belief in the difficulty of treating the condition is exaggerated. Successful treatment demands, however, not only some knowledge of the use of insulin but the ability to prescribe the quantities of calories and proximate principles suitable for the patient. Just as when a doctor prescribes doses of certain drugs and his prescription is made up for him by a pharmacist, so his dietetic prescription can be turned into terms of actual foodstuffs by a dietitian. A dietitian, however, is not always available, and in the following pages an attempt has been made to describe a simple dietetic system which should suffice for the treatment of the average diabetic.

The Caloric Value of the Diet.—Many people in this country eat more food than is necessary for them to maintain their weight and to give them energy for their various activities In a few unfortunate individuals these excess [illegible]

[illegible] therefore, of diabetic dieting consists in cutting out the excess food consumption in which many indulge. In other words, we should give the diabetic sufficient calories, and no more, to give him energy for his particular activities and to maintain him at his ideal weight, or slightly below it, for no diabetic should be allowed to become overweight.

It is apparent that the number of calories required will vary considerably according to the age, sex, weight, height and particular activities of the diabetic concerned. For example, an elderly, small, fat female of sedentary habit will require considerably fewer calories than a young, tall, underweight, hardworking male. The first will probably benefit by being given a 1,000 or 1,200 Cal diet to bring her down to near her ideal weight, and will thereafter require not more than about *1,600 or 1,800 Cals to maintain her at that weight, and to* satisfy her moderate energy requirements. The second, on the other hand, may [illegible] Cals. to bring him up to near his ideal weight [illegible] should be given only in exceptional circumstances), and he may thereafter require some 2,500 Cals. to maintain him at that new level and to give him energy for his strenuous life. In between these two extremes lie the majority of diabetics, who will thus require diets varying in caloric value between 1,800 and 2,500 according to the particular circumstances of the case.

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possible limits consistent with the [illegible] aim of dietetic treatment in the pre[illegible]d for a *good many years after* its discovery. Diets then rarely co[illegible] as 100 g. of carbohydrate and their [illegible]rtion of fat [illegible] unappetizing and somewhat nauseatin[illegible]

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relatively higher calories are needed, 180 to 220 g of carbohydrate should be given.

The Fat and Protein Content of the Diet.—Of late years there has been a tendency in many schools to break away from the extremely meticulous dietetic directions of the past as regards protein and fat and to adopt a *laisser-faire* attitude in regard to these constituents of the diabetic's diet. The rule of several dietetic systems has been "take care of the carbohydrate and the protein and fat will take care of themselves" We believe this attitude to be exaggerated In the past dietetic directions regarding protein and fat may have been unduly meticulous, but to disregard them altogether is undesirable. To obtain the best results, carbohydrate, protein and fat should all be accurately

in the first few weeks a most tedious and time-consuming exercise becomes eventually a simple matter of habit which need not handicap the individual concerned to any significant extent

The Calculation and Prescription of the Diet.—The following table

shows an undesirable gain in weight.

	Cals.	*CHO*	*Prot.*	*Fat.*
		g.	g	g.
Small sedentary woman	1780	150	70	100
Person of average build and activity	2200	180	90	125
Big hard-working man . .	2500	225	107	130

an exceptional case, and apart from the child diabetic, the surgical diabetic and the diabetic complicated by infection, this belief in the difficulty of treating the condition is exaggerated. Successful treatment demands, however, not only some knowledge of the use of insulin but the ability to prescribe the quantities of calories and proximate principles suitable for the patient. Just as when a doctor prescribes doses of certain drugs and his prescription is made up for him by a pharmacist, so his dietetic prescription can be turned into terms of actual foodstuffs by a dietitian. A dietitian, however, is not always available, and in the following pages an attempt has been made to describe a simple dietetic system which should suffice for the treatment of the average diabetic.

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The Carbohydrate Content of the Diet.—Since carbohydrate is the food which diabetics have most difficulty in metabolizing, it would at first hand appear reasonable to reduce the carbohydrate content of the diet to the lowest possible limits consistent with the avoidance of ketosis. This was indeed the [illegible] years after [illegible] rbohydrate [illegible] somewhat nauseating.

Nowadays we realize that it is undesirable for the carbohydrate in diabetic diets to be so rigorously restricted. Patients feel better on a more liberal allowance and the diets so constructed are much pleasanter to take. Further, [illegible] intake are [illegible] is made. [illegible] duration

of the blood glucose curve is conditioned by the constitution of the diet which the patient has been taking previously; after a period on a low carbohydrate diet, ingestion of glucose leads to a much higher and more prolonged rise in the blood glucose than is the case when the subject has been taking a normal carbohydrate intake. This suggests that carbohydrate is a stimulus to insulin formation, and if it is too rigorously controlled in the diabetic a further inhibition of an already poor supply may occur

We believe that the *average* diabetic in this country requires for maintenance 145 to 220 g. of carbohydrate a day, depending on his caloric requirement. When this is low, 145 to 160 g. of carbohydrate is usually sufficient; when relatively higher calories are needed, 180 to 220 g. of carbohydrate should be given.

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The Calculation and Prescription of the Diet.—The following table gives a rough approximation of the calories and proximate principles which will be required by persons varying in their build and physical activities. Such prescriptions will require to be modified according to the individual reaction to the diet. If the patient is unduly hungry or loses weight on the diet, it will have to be appropriately increased, and *vice versa* if the patient finds it excessive or shows an undesirable gain in weight

	Cals.	*CHO.*	*Prot.*	*Fat.*
		g	g	g
Small sedentary woman	1780	150	70	100
Person of average build and activity	2200	180	90	125
Big hard-working man	2500	225	107	130

Diabetics can be divided roughly into two main groups. On the one hand there are the obese, middle-aged or elderly diabetics showing little sensitivity to insulin or liability to develop ketosis On the other hand there are the thin

an exceptional case, and apart from the child diabetic, the surgical diabetic and the diabetic complicated by infection, this belief in the difficulty of treating the condition is exaggerated. Successful treatment demands, however, not only some knowledge of the use of insulin but the ability to prescribe the quantities of calories and proximate principles suitable for the patient. Just as when a doctor prescribes doses of certain drugs and his prescription is made up for him by a pharmacist, so his dietetic prescription can be turned into terms of actual foodstuffs by a dietitian A dietitian, however, is not always available, and in the following pages an attempt has been made to describe a simple dietetic system which should suffice for the treatment of the average diabetic.

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Vegetables

(When fresh vegetables are unobtainable, tinned ones may be substituted)

Group I—

1 *to* 3 *per cent. Carbohydrate* :

Mushrooms (no food value)	Cauliflower.	Cucumber.
Mustard and cress.	Artichokes.	Vegetable marrow.
Watercress	Seakale.	Tomatoes.
Lettuce.	French beans.	Brussels sprouts
Curly greens	Eggplant.	Endive.
Celery.	Salsify	Leeks
Spinach.	Asparagus	Rhubarb cooked with a pinch of baking soda.
Cabbage.	Radishes.	

Group II—

3 *to* 6 *per cent Carbohydrate* ·

Turnips	Onions.	Carrots

Group III—

10 *per cent. Carbohydrate*

Beetroot	Parsnip.	Fresh peas.

20 *per cent Carbohydrate* (*do not take without permission*) :

Potato	Cooked dried peas, beans, lentils.

Fruits

(No tinned fruits)

4½ *Oz.* 7½ *Per Cent Fruit*	= 3½ *Oz* 10 *Per Cent Fruit*	= 2¼ *Oz.* 15 *Per Cent Fruit*	= 1¾ *Oz.* 20 *Per Cent. Fruit*
Grapefruit.	Gooseberries	Apple	Figs, dried.
Strawberries	Orange	Pear	Prunes, dried.
Blackberries	Peach	Apricots, dried.	Bananas.
Red currants	Pineapple	Plums, Victoria +stone.	
Black currants	Greengage+stone	Grapes.	
White currants	Cherries+stone.	Nectarine+stone.	
Cranberries	Damson+stone		
Raspberries	Tangerines		
Loganberries.	Apricots (fresh)		
Melon.			

It is, of course, of the utmost importance to study the character of the patient concerned. There are many who require to be warned continually of the necessity of dietetic care, and may indeed occasionally have to be frightened into being more accurate by a lecture on the considerable risk which they run by non-observance of the rules Such treatment in other patients would turn them into hypochondriacs. Some over-anxious diabetics require the disease and its dangers to be minimized rather than stressed. Such patients should be encouraged to consider diabetes as an inconvenient idiosyncrasy rather than as a

foodstuff, but, when the natural variation of food composition is taken into account, the result is accurate enough for all practical purposes.

EXCHANGES FOR BREAD

Food	*Weight* Oz.	*Approximate Amount*
Bread	1	1 thin slice.
Rich tea biscuits	—	2.
Ryvita	—	2 squares.
Water biscuits	—	3.
Oatcake	1	3 small round.
Cooked potato	2½	1 rounded tablespoonful.
Macaroni (boiled)	3½	1 teacup.
Rice (uncooked)	½	3 teaspoonfuls.
Rice (boiled)	1½	2 tablespoonfuls.
Cereal pudding (no added sugar)	4	4 level tablespoonfuls.
Cornflakes	¾	1 scant teacup.
Porridge	—	3 tablespoonfuls.
Orange or other 10 per cent. fruit	5	1 large.
Apple or other 15 per cent. fruit	3½	1 small.

EXCHANGES FOR MEAT (COOKED)

Food	*Weight* Oz.	
Meat (any medium fat beef, lamb, mutton, pork)	1	
Chicken or rabbit	1½	
Liver or kidney or sweetbread	1½	
Tripe	2	
Tongue	1	
Cold ham	1	
White fish	1½	+¼ oz. margarine.
Finnan haddock	1½	+¼ oz. margarine.
Cod roe	1	+¼ oz. margarine.
Herring	1½	
Salmon, tinned or fresh	1½	
Sardines	1	3 medium
Bacon	1½	−½ oz. margarine
Egg	1	whole.
Cheese	¾	

EXCHANGES FOR BUTTER

Food	*Weight* Oz.	
Butter or margarine	½	
Cream, 20 per cent. (thin)	2	
Cream, 40 per cent. (thick)	1	
Mayonnaise	¾	1 tablespoonful.
Olive oil	⅓	

VEGETABLES

(When fresh vegetables are unobtainable, tinned ones may be substituted)

Group I—

1 *to* 3 *per cent. Carbohydrate* .

Mushrooms (no food value)	Cauliflower.	Cucumber.
Mustard and cress.	Artichokes.	Vegetable marrow.
Watercress.	Seakale.	Tomatoes.
Lettuce.	French beans.	Brussels sprouts.
Curly greens.	Eggplant	Endive.
Celery.	Salsify.	Leeks.
Spinach.	Asparagus	Rhubarb cooked with a pinch of baking soda
Cabbage.	Radishes.	

Group II—

3 *to* 6 *per cent. Carbohydrate* ·

Turnips.	Onions.	Carrots

Group III—

10 *per cent. Carbohydrate*

Beetroot	Parsnip.	Fresh peas.

20 *per cent Carbohydrate* (*do not take without permission*) ·

Potato	Cooked dried peas, beans, lentils

FRUITS

(No tinned fruits)

4½ *Oz.* 7½ *Per Cent Fruit*	= 3½ *Oz.* 10 *Per Cent Fruit*	= 2¼ *Oz.* 15 *Per Cent. Fruit*	= 1¾ *Oz.* 20 *Per Cent. Fruit*
Grapefruit.	Gooseberries	Apple	Figs, dried.
Strawberries	Orange	Pear.	Prunes, dried.
Blackberries	Peach	Apricots, dried.	Bananas
Red currants	Pineapple	Plums, Victoria +stone.	
Black currants.	Greengage+stone.	Grapes.	
White currants	Cherries+stone.	Nectarine+stone.	
Cranberries	Damson+stone		
Raspberries	Tangerines.		
Loganberries.	Apricots (fresh).		
Melon.			

It is, of course, of the utmost importance to study the character of the patient concerned. There are many who require to be warned continually of the necessity of dietetic care, and may indeed occasionally have to be frightened into being more accurate by a lecture on the considerable risk which they run by non-observance of the rules Such treatment in other patients would turn them into hypochondriacs. Some over-anxious diabetics require the disease and its dangers to be minimized rather than stressed Such patients should be encouraged to consider diabetes as an inconvenient idiosyncrasy rather than as a

night. The hyperglycæmia occurring after breakfast in such patients can be controlled by giving a dose of soluble insulin along with the ZPI in the morning, and this combination is probably the ideal method for the control of more severe cases. *In severe cases the morning ZPI may fail to control the* after-supper hyperglycæmia, and a second injection of soluble insulin will have to be given in the evening.

Globin insulin is prepared by combining insulin with globin, a protein obtained from red blood cells after removal of the chromogen fraction. A clear solution is formed to which a trace of zinc is added. Its effect is maximal in from five to eight hours after injection, and is completely exhausted in about fourteen hours. Its action is thus intermediate between soluble insulin and ZPI—much slower and more prolonged than the former and more rapid and transient than the latter. Though some cases of mild diabetes are effectively

prolongation of their action on the absorption of insulin on to a foreign protein More recently it has been shown that small quantities of zinc delay the rate at which insulin crystals dissolve and so prolong their action without the addition of foreign protein substances, provided the zinc insulin crystals are suspended in an acetate and not in a phosphate or citrate buffer. The duration of action of the zinc insulin suspensions depend also on the size and form of the insulin particles. If the particles are crystalline, the action of the suspension is prolonged up to thirty hours, but if they are amorphous, the duration of action is limited to from twelve to sixteen hours. Two zinc insulin suspensions of this nature have been manufactured with different speeds and duration of action. The crystalline form (ultra-lente) has an even more prolonged effect than ZPI, while the amorphous form (semi-lente) has a more rapid, stronger and shorter action comparable to that of globin insulin. A mixture of seven parts of ... patients, combining as it does

...ensions

...stalline

...suit the

particular requirements of any given patient; but these suspensions must not be mixed with soluble insulin, as the latter, being acid, changes the *p*H of the suspension and alters the size and form of the insulin particles.

Since the suspensions *contain no foreign protein*, they seldom cause ... phenomena, which are not at all uncommon with ZPI and globin

even the few

...arations with-

...en intractable

sensitization phenomena are encountered. In severe cases, however, they are ... mild

The action of the various insulins is summarized in the following ... must be remembered that the larger the dose of any preparation given, the longer it acts.

Type of Insulin	*Maximum Action in Hours*	*Duration of Action in Hours*
1. Quick Acting—		
Soluble . .	2-6	4-8
2. Intermediate Acting—		
(*a*) Globin .	6-8	8-14
(*b*) IZS Amorphous (semilente)	8-12	14-18
3. Long Acting—		
(*a*) ZPI . . .	8-12	14-24
(*b*) IZS Crystalline (ultralente)	10-14	18-30
4 Mixtures—		
(*a*) ZPI and soluble		
(*b*) IZS (lente) . 30 per cent. amorphous, 70 per cent. crystalline.		

Technique of Administration.—All the insulins referred to above are supplied in two strengths—40 units and 80 units to the ml When only a small [illegible]

strength as well. This weak preparation is never required for therapeutic purposes, and its existence merely causes confusion.

It is very desirable that an insulin syringe graduated in units, rather than an ordinary 1 ml or minim syringe, should be used, especially when the patient is going to administer the drug himself. It is a more accurate method and saves [illegible]

selves. This is of the utmost importance, as it makes the patient much more independent and saves an infinity of bother A great deal of encouragement, a little mild bullying and most patient explanations are sometimes necessary to begin with. If this initial trouble is taken, it is only very little children, the senile, [illegible]

Cases of sepsis as the result of insulin injections, though rare, occasionally occur with ZPI and globin insulin, which may give rise to subcutaneous abscesses in spite of the fact that aseptic precautions seem to have been taken at the injection [illegible]

Methylated spirit is often used instead of surgical spirit, the only drawback to it

night. *The hyperglycæmia occurring after breakfast* in such patients can be controlled by giving a dose of soluble insulin along with the ZPI in the morning, and this combination is probably the ideal method for the control of more severe cases. In severe cases the morning ZPI may fail to control the after-supper hyperglycæmia, and a second injection of soluble insulin will have to be given in the evening.

Globin insulin is prepared by combining insulin with globin, a protein obtained from red blood cells after removal of the chromogen fraction. A clear solution is formed to which a trace of zinc is added. Its effect is maximal in from five to eight hours after injection, and is completely exhausted in about fourteen hours. Its action is thus intermediate between soluble insulin and ZPI—much slower and more prolonged than the former and more rapid and transient than the latter. Though some cases of mild diabetes are effectively [illegible]

Insulin Zinc Suspensions (IZS). Both ZPI and globin insulin depend for the [illegible]

in an acetate and not in a phosphate or citrate buffer. The duration of action of the zinc insulin suspensions depend also on the size and form of the insulin particles. If the particles are crystalline, the action of the suspension is prolonged up to thirty hours, but if they are amorphous, the duration of action is limited to from twelve to sixteen hours. Two zinc insulin suspensions of this nature have been manufactured with different speeds and duration of action. [illegible] prolonged effect than ZPI, [illegible] , combining as it does [illegible] of both suspensions. [illegible] ong-acting crystalline [illegible] mixture to suit the particular requirements of any given patient; but these suspensions must not be mixed with soluble insulin, as the latter, being acid, changes the *p*H of the suspension and alters the size and form of the insulin particles.

Since the suspensions contain no foreign protein, they seldom cause [illegible] phenomena which are not at all uncommon with ZPI and globin [illegible] he few [illegible] with- out trouble. The suspensions are thus [illegible] ctable [illegible] In severe cases, however, they are [illegible]

The action of the various insulins is summarized in the following [illegible] must be remembered that the larger the dose of any preparation given, the longer it acts.

Type of Insulin	*Maximum Action in Hours*	*Duration of Action in Hours*
1. Quick Acting—		
Soluble	2-6	4-8
2. Intermediate Acting—		
(*a*) Globin	6-8	8-14
(*b*) IZS Amorphous (semi-lente)	8-12	14-18
3. Long Acting—		
(*a*) ZPI	8-12	14-24
(*b*) IZS Crystalline (ultra-lente)	10-14	18-30

4. Mixtures—
   (*a*) ZPI and soluble
   (*b*) IZS (lente). 30 per cent. amorphous, 70 per cent. crystalline.

Technique of Administration.—All the insulins referred to above are supplied in [illegible]
dose of 20 [illegible]
When large [illegible]
used so as [illegible]
injection. [illegible]
strength as [illegible]
purposes, and its existence merely causes confusion

[illegible]

selves. This is of the utmost importance, as it makes the patient much more independent and saves an infinity of bother. A great deal of encouragement, a little mild bullying and most patient explanations are sometimes necessary to [illegible]

When reasonable control of a patient's glycosuria has been established, the urine tests need only be made on the early morning and night specimens; and when thorough stabilization has been achieved the occasional testing of a twenty-four-hour specimen is all that is necessary.

Control of a Moderate Case by Insulin.—A new case of diabetes, provided the condition is not severe and no ketosis is present, can be started on IZS (lente). It takes longer to control a case by this method, which is, however, simpler as no conversion from one insulin to another is involved. Twelve or 16 units can be given to begin with, and this dose can be increased appropriately by 4 units at a time until reasonable control is established. Unless the patient is under close observation in hospital it is wise to allow three or four days to elapse between each increase in dose.

Although IZS is the insulin of choice for the control of mild to moderate [illegible]

[illegible]

Hypoglycæmia.—An overdose of insulin results in an undue lowering of [illegible]

[illegible]

concentration of as low as 50 to 60 mg. per 100 ml. is usually necessary to [illegible]

[illegible]

ness and emptiness about the pit of the stomach. Tremor and tachycardia are common and diplopia occasionally occurs. The individual feels faint and dizzy and often experiences a strong desire for food. Clammy sweating is almost invariable, and, as the condition becomes more pronounced, mental symptoms are common, the patient sometimes becoming very hysterical—laughing, crying, shouting and struggling. Diabetics, while hypoglycæmic, may run amuck in the streets and be apprehended by the police as drunk and disorderly. At other times lassitude and somnolence are more marked features, especially in children. The advanced stages of hypoglycæmia are characterized by muscular twitchings, deepening coma and eventually by convulsions.

Reactions with depot insulins may be more severe than with soluble insulin and more difficult to treat, the patients tending to slip back again into coma after they have been brought out of it, unless large amounts of glucose are given. Further, the reactions may differ symptomatically from those due to soluble insulin. Many of the symptoms of soluble insulin hypoglycæmia are due to endogenous adrenaline which is secreted in an attempt to raise the blood glucose. In consequence sweating, palpitation and tremors are its characteristic features. Hypoglycæmia produced by depot insulins, on the other hand, comes on so slowly that this outpouring of endogenous adrenaline does not occur to the same extent, and general malaise, nausea, vomiting and headache are the symptoms most commonly experienced. Patients should be warned of these novel features of hypoglycæmia before being given depot insulins, since failure to recognize the symptoms as being due to hypoglycæmia may prevent them from taking appropriate measures and a severe hypoglycæmic coma may ensue.

The more severe hypoglycæmic symptoms seldom manifest themselves for at least a quarter of an hour after the initial sensations have been experienced. Thus, the patient has usually plenty of time to rectify matters. The treatment consists, of course, in raising the blood glucose by the administration of carbohydrate This can be done most conveniently and simply by expediting the next meal, for in this way there is no disturbance of the patient's carbohydrate and calorie intake for the day. Hypoglycæmia does not, however, invariably occur under circumstances in which a meal can be taken. All patients, therefore, who are taking insulin should invariably carry about with them several lumps of sugar. After taking sugar the patient should remain as quiet as possible till the symptoms have disappeared, as exercise exacerbates the tendency to hypoglycæmia. A drink of water should be taken with the sugar to facilitate its rapid absorption. If the symptoms do not quickly disappear, or should they become worse, another two lumps of sugar can be taken The object should be to banish the symptoms with the smallest effective quantity of sugar in order not to disturb [illegible]

than sugar or orange juice.

In the great majority of cases these measures are rapidly effective. Occasionally, however, a patient is encountered in deep hypoglycæmic coma and unable to swallow In such circumstances a subcutaneous injection of 0 5 ml. of adrenaline (solution 1 : 1,000) should be given. This converts any available glycogen into glucose, thereby raising the blood glucose This procedure is usually effective in rousing the patient from his coma sufficiently to permit him to swallow carbohydrate food, which should be given, if possible, in the form of glucose or sugar in orange juice. An intravenous injection of 50 ml. of 25 per cent glucose solu[illegible]
oz.) of water by [illegible]
may occasionally [illegible]
giving of rectal glucose-saline, which is sometimes advocated, is a very slow and uncertain method of raising the blood glucose and is not to be recommended in such emergencies

All patients taking insulin should have the symptoms of hypoglycæmia carefully explained to them, and should be thoroughly conversant with the necessary treatment. Such patients should carry a card giving their name and address, the telephone number of their doctor or diabetic clinic, their dose of insulin and the need to give them sugar if they are discovered in a faint or ill condition A suitable card of this nature is supplied by the Diabetic Association. Some careless patients who do not take their disease sufficiently seriously may have to have the dangers of hypoglycæmia stressed to them. We believe, however, that many doctors overstress the dangers of hypoglycæmia, causing their patients to become unduly alarmed about it. This exaggerated terror of hypoglycæmia is often responsible for inadequate dosage, or even for insulin [illegible]

not exceeding 175 mg. per 100 ml. should be regarded as satisfactory; higher figures suggest an appropriate increase in the dose of insulin.

THE TREATMENT OF DIABETIC COMA

Diabetic coma is practically always preventable, and should not occur when an intelligent patient is under efficient treatment. Occasionally it may be encountered in an undiagnosed—and therefore untreated—case; sometimes it is due to simple disregard of treatment by the patient or to grossly ineffective treatment by the doctor; more often it is the result of gastro-intestinal upsets, infections or surgical operations in diabetics who are being adequately treated for all ordinary occasions but whose treatment is insufficiently elastic to cope with such emergencies.

when skilled institutional treatment can be procured, the patient should be transferred to hospital after first-aid treatment in the form of an adequate injection of insulin has been given by the practitioner.

The principles of treatment in diabetic coma are to eradicate the ketosis by giving soluble insulin, to combat the invariable dehydration and circulatory collapse by giving fluids and to administer potassium salts during the recovery phase so as to prevent serious hypopotassæmia. In addition, it is wise to wash out the stomach, to evacuate the bowel and to treat any associated infection which may have precipitated the coma

Insulin.—It is insufficiently appreciated that diabetic coma requires a large quantity of insulin for its successful treatment. Further, the insulin should be used in large doses in the first few hours of treatment rather than in moderate amounts spread over twenty-four hours. Soluble insulin should be used invariably, since depot insulins, owing to their slow action, are entirely unsuited to cope with the emergency of diabetic coma. From 500 to 700 units, or even more, may have to be administered in the twenty-four hours to patients in severe diabetic coma, but the major portion of this should be given in the first few hours of treatment. Thus from 75 to 100 units should be given as an initial dose, depending on the severity of the case, 30 to 50 of which can be given intravenously, as the absorption of insulin from the subcutaneous tissues may, in a severe case, be very slow owing to the shocked state of the patient. A further 50 to 100 units should be given subcutaneously an hour and a half, and three hours, later. Thus from 175 to 300 units, depending on the severity of the case, should be injected in the first three hours of treatment. Thereafter appropriately smaller doses with longer intervals between them can be administered till the ketosis has been satisfactorily controlled

Too often quite insufficient doses of insulin are administered in this emergency from fear of inducing hypoglycæmia. There is little danger of this in the early stages, and it is unnecessary and even undesirable to " cover " these initial doses with glucose, which used to be thought such an essential part of the

theoretical considerations, however, ignore the fact that a patient in diabetic coma is extremely resistant to insulin Hence in the early stages of treatment large doses can be given freely without much danger of the patient slipping imperceptibly from the coma of ketosis to that of hypoglycæmia, provided the urine is tested prior to each injection and a large quantity of glucose is found to be present. The objective is a rapid reduction of the ketonuria with a slower decrease of the glycosuria It is, of course, almost essential to have in addition frequent estimations of the blood glucose. When this is possible, the dose of

the dry skin, leathery tongue, and collapsed veins of the patient, and in the profound fall in blood pressure and intraocular pressure which also occur The correction of this dehydration and its associated circulatory collapse is almost as important as the treatment of the ketosis itself, but it is often forgotten or treated inadequately.

desirable and in severe cases essential to augment the fluid intake by an intravenous drip. Two litres of normal saline should be administered by this method in the first three hours of treatment If the patient is still dehydrated at the end

unfortunately so collapsed that it may occasionally be impossible to administer transfusions without cutting down upon one of them and inserting a cannula The rectal administration of fluids is a most unsatisfactory substitute for intravenous-drip transfusion and is not to be recommended in this emergency

Potassium.—The danger of hypopotassæmia in diabetic ketosis following therapy with insulin, saline and glucose has been stressed elsewhere (see p. 111). Before treatment the serum potassium level is usually normal, despite the loss of potassium caused by the acidosis As the result of the institution of insulin therapy and the treatment of the dehydration, however, potassium passes from the extracellular to the intracellular fluids and the serum potassium may fall to extremely low levels Thus deaths from hypopotassæmia may occur during

p. 111.

Diet.—After the first three hours of intensive treatment by insulin and fluid the patient will usually have recovered sufficiently to permit of oral feeding,

which should be started as soon as possible. Twenty-five grammes of glucose solution, or equivalent feeds of common carbohydrate foodstuffs (see p. 319), should be given every two hours until the patient is fit for a more ordinary diet It should be remembered in selecting the appropriate food that strong sugar

found suitable for cases of diabetic ketosis in danger of coma and for diabetics temporarily unfit to take their ordinary diet owing to gastro-intestinal upsets or intercurrent infections. As long as the ketonuria is controlled, no serious attempt need be made at this stage to get the patient "sugar-free" till he is again

pulse rate has become normal In many cases this may take a week or more.

DIABETES IN CHILDREN

Diabetes may occur at any age, but it is relatively uncommon in children, especially in young children. This is fortunate, for the treatment of the diabetic ... a variety of reasons It is ... on a standard diet and a ... he case of an adult, for the child's nutritional needs are continually altering according to his changing development

To provide for his growth and energy requirements, a child needs relatively higher diets than an adult in respect of protein, carbohydrate and total calories, and a generous supply of milk must be given. A high fat intake, however, especially in young children, is often poorly tolerated, producing ketosis and fatty stools and large quantities of green vegetables are often insufficiently ... his ... may ... by ... variation in their physical activity from day to day. Thus the passionate ... es, which ... ir glucose tolerance. Insulin used often acts more ... in adults, producing an unusually rapid fall in the blood glucose level to be succeeded by an equally rapid rebound. Again, children are more liable to infectious diseases than adults, and infections, as we have seen, are the bugbear of diabetics. Lastly, few children suffer from mild diabetes, but usually from an acute type of the disease, showing a marked tendency to ketosis. For these reasons insulin is an invariable necessity for child diabetics, who cannot tolerate without its help diets ... growth, ... ns ... 10 ... ly ... 's adults. It is important to take the child himself into the ... councils, to treat him as an intelligent person and to give him a sense of

TABLE II

Age (Years)	*Calories per Kilogram Body-weight* *	*Grammes of Protein per Kilogram Body-weight* †
1	90 to 100	3·5
2		
3	80 to 90	3·0
4		
5		
6	70 to 80	2·5
7		
8		
9		
10	Girls, 60 to 70 Boys, 65 to 75	
11		
12		
13		
14	Girls, 40 to 60 Boys, 50 to 65	2·0
15		
16		
17		1·5
18		

* From Rose's "Laboratory Handbook for Diabetics"
† From the Report on the Physiological Basis of Nutrition drawn up by the Technical Commission of the Health Committee of the League of Nations.

Minerals and Vitamins.—It is very important that the diabetic child

DIABETIC DIET FOR CHILD AGED 3 TO 4 YEARS

C 135 g P. 50 g F 63 g. Cals 1,307

Breakfast—
Porridge, 3 tablespoonfuls, or exchange.
Milk from allowance.
Bread, 1 oz.
Butter from allowance.

Dinner—
Cooked meat, 1 oz, or exchange.
Small helping of vegetable—see list.
Potato, 2½ oz.
Orange, 3½ oz., or exchange—see list
Milk to drink from allowance.

Tea—
Bread, 1½ oz.
Butter from allowance.
1 egg or exchange
Tomato and lettuce as desired
Milk from allowance

Supper—
Bread, 1 oz.
Butter from allowance
Milk from allowance
10 per cent. fruit, 3½ oz , or exchange—see list.

Daily allowance—Milk—1 pint.
Butter or margarine—1 oz

DIABETIC DIET FOR CHILD AGED 7 TO 8 YEARS
C 160 g P 70 g. F. 92 g. Cals 1,748

Breakfast—
Bacon, 1 oz.
Bread, 2 oz
Butter from allowance.
Milk from allowance

Mid-morning—
Milk from allowance, now or later

Dinner—
Clear soup or Marmite if desired (diced vegetable may be added).
Cooked meat, 1½ oz , or exchange.
Average helping of 3 per cent vegetable—see list.
Potato, 2½ oz , or exchange.
Milk from allowance—may be used as curds with chocolate or vanilla flavouring, or as custard, using an egg from another meal.
10 per cent fruit, 3½ oz.—see list.

Tea—
Bread, 2 oz.
Butter from allowance.
1 egg or exchange.
Tomato and lettuce as desired
Milk from allowance

Supper—
Bread, 1½ oz.
Butter from allowance.
Milk from allowance.
10 per cent fruit, 3½ oz.—see list.

Daily allowance—Milk—1⅓ pints.
Butter or margarine—1¼ oz.

To *decrease* this diet to 145 *C., Cals,* 1,520, making it suitable for children aged 5 to 6 years, OMIT 1 oz. bread and 1 oz. bacon

To *increase* this diet to 175 *C., Cals.* 1,990, ADD 1 oz. bread, ½ oz. butter, ½ oz. bacon.

DIABETIC DIET FOR CHILD AGED 11 TO 12 YEARS

C. 200 g. P. 88 g. F. 110 g. Cals. 2,132

Breakfast—
Egg or exchange (p. 294).
Bread, 2½ oz.
Butter from allowance.
Milk from allowance.

Mid-morning—
Milk from allowance now or later.

Dinner—
Clear soup or Marmite if desired (diced vegetables may be added).
Cooked meat, 2 oz., or exchange.
Average helping of 3 per cent. vegetable—see list (p. 295).
or 1 tablespoonful of 6 per cent. vegetable—see list.
Potato, 5 oz , or exchange.
Milk from allowance may be used as curds (junket) with chocolate or vanilla flavouring, or as custard, using an egg in exchange for 1 oz. meat at any other meal.
10 per cent fruit, 3½ oz —see list.

Tea—
Bread, 2½ oz
May be used as sandwich with filling of tomato, lettuce, cress or a little grated cheese.
Tea or milk from allowance.

Supper—
Cooked meat, 2 oz., or exchange.
Tomato or other vegetable as desired.
Bread, 2 oz.
Butter from allowance
Milk from allowance.
10 per cent. fruit, 3½ oz —see list

Daily allowance—Milk—1⅓ pints.
Butter or margarine—2 oz.

To increase this diet any of the additions from the exchange lists (pp. 294, 295) may be added.

DIABETES AND PREGNANCY

In the pre-insulin era pregnancy was a very rare event in a diabetic woman; the majority of such women of childbearing age died within a short time of developing the disorder; and during their brief lives they were usually amenorrhœic and therefore infertile. Treatment with insulin, by preserving their lives and abolishing their amenorrhœa, has raised the status of the pregnant diabetic from that of a medical curiosity to one for which special provision must be made in any maternity service

When pregnancy did occur in a diabetic woman in the pre-insulin era death from diabetic coma usually resulted or, if she survived, the child was born dead. Although insulin treatment rendered pregnancy relatively safe for the mother, the fœtal loss rate remained for a long time distressingly high at about 40 per cent. If, however, the mother is meticulously supervised by both physician and obstetrician during pregnancy, if the child is delivered electively prior to full term and if close co-operation between physician, obstetrician, anæsthetist and pædiatrician is obtained, the loss can then be reduced to less than 20 per cent.

appropriate adjustments in her insulin dosage The renal threshold for glucose is commonly much lowered in pregnancy so that allowance may have to be made for this in the interpretation of urine tests, for this reason, while the patient is

i should be obtained,
ascertained and the
Once the physician
is satisfied that the patient is thoroughly conversant with the principles of maintaining good dietetic and insulin control she may be discharged from

and evening specimens of urine for glucose and to bring a record of the results

should be no hesitation in prescribing an additional dose of soluble insulin before tea or supper if this proves necessary.

At the 30th or 31st week the patient should be readmitted to hospital. She should not be confined strictly to bed and a moderate degree of gentle exercise should be taken. During this time diabetic control must be meticulously

pregnancy. When hydramnios is present its progress can often be satisfactorily controlled by the injection of mersalyl two or three times a week. Acute hydramnios is, however, an indication for the emergency delivery of the child by Cæsarean section in the hope that it will be sufficiently mature to survive.

bility of obstetrician and physician. It is, however, not unusual for the mother to anticipate events by going into labour spontaneously. In such circumstances, in primiparous patients or in those with large babies, Cæsarean section should be undertaken as an emergency operation.

When elective operative delivery is planned the patient must be prepared

this stage a short anæsthesia of the patient by thiopentone is ideal

Some authorities advocate delivery by the vaginal route if the baby is of normal size; this can seldom be achieved—especially in primigravidæ—without

in addition, metabolic

se reasons, and because

ginal delivery is seldom

advisable.

The care of the baby should ideally be supervised by a pædiatrician The infant—particularly when small—should be regarded as physiologically pre-

mature and should be nursed for the first forty-eight hours by the trained staff of the premature baby unit. During this time no feeds should be given and oxygen administration may be required. Neo-natal hypoglycæmia is not now regarded as a cause of death in these babies and the former practice of giving them parenteral glucose has been abandoned. A free diuresis occurs in the babies of diabetic mothers—particularly in the large ones—resulting in a considerable loss of weight in the first few days.

adequate supper prior to which insulin may be given. On the following day her ordinary diet can often be tolerated. Insulin requirements fall considerably

given and the daily diet reduced to that taken prior to pregnancy. Following discharge from hospital the patient should be seen at fortnightly intervals for a month or two to ensure that the diabetic control is satisfactory.

Priscilla White's claim that the fœtal mortality in diabetic pregnancy can be greatly reduced by the administration of large doses of stilbœstrol during pregnancy has not been generally confirmed: it is probable that the excellent results obtained in her clinic are due more to the superb diabetic, obstetric and *pædiatric management of her patients than to the hormonal therapy employed.*

Diabetes *per se* does not constitute an indication for therapeutic abortion, though the presence of severe diabetic nephropathy or retinopathy may do so. Nevertheless, in respect of ultimate longevity, pregnancy constitutes a hazard to the diabetic mother and many authorities advocate sterilization after the second or third delivery—or earlier if the patient is no longer young and exhibits

Should this contain more than 120 mg. per 100 ml. of glucose a full glucose tolerance test must be undertaken. Even if this gives normal results it is wise to regard the patient as pre-diabetic and to keep her under careful observation from this point of view should she have a previous obstetric history suggestive of diabetes.

should be no hesitation in prescribing an additional dose of soluble insulin *before tea or supper if this proves necessary.*

At the 30th or 31st week the patient should be readmitted to hospital. She should not be confined strictly to bed and a moderate degree of gentle exercise should be taken During this time diabetic control must be meticulously maintained, the insulin dosage being based on frequent estimations of the blood glucose values. The incidence of toxæmia of pregnancy in diabetic women has been exaggerated, but hydramnios is so common that the salt intake of diabetic women should be drastically restricted during the last few weeks of their pregnancy. When hydramnios is present its progress can often be satisfactorily controlled by the injection of mersalyl two or three times a week. Acute hydramnios is, however, an indication for the emergency delivery of the child by Cæsarean section in the hope that it will be sufficiently mature to survive. [illegible] considerable risk of [illegible] is [illegible] it [illegible] it [illegible] ie [illegible] ly [illegible] o [illegible] et [illegible] id [illegible] er [illegible] i- bility of obstetrician and physician. It is, however, not unusual for the mother to anticipate events by going into labour spontaneously. In such circumstances, in primiparous patients or in those with large babies, Cæsarean section should be undertaken as an emergency operation

When elective operative delivery is planned the patient must be prepared properly. The dose of long-acting insulin given the previous morning should be adjusted so that the blood glucose concentration on the morning of operation lies between 130 and 150 mg. per 100 ml.; no food or fluids should be given on the morning of operation, nor should any drug likely to depress the respiratory [illegible] seldom necessary to [illegible] nship [illegible] ect it [illegible] f the [illegible] d by lower segment Cæsarian section unless the patient is to be sterilized, when the classical operation is performed. When spinal anæsthesia is employed retching or vomiting almost invariably occurs within five minutes of delivery so that at this stage a short anæsthesia of the patient by thiopentone is ideal.

Some authorities advocate delivery by the vaginal route if the baby is of normal size; this can seldom be achieved—especially in primigravidæ—without [illegible] the respiratory centre and in addition, metabolic [illegible], and because [illegible] ery is seldom advisable.

The care of the baby should ideally be supervised by a pædiatrician. The infant—particularly when small—should be regarded as physiologically pre-

mature and should be nursed for the first forty-eight hours by the trained staff of the premature baby unit. During this time no feeds should be given and oxygen administration may be required. Neo-natal hypoglycæmia is not now regarded as a cause of death in these babies and the former practice of giving them parenteral glucose has been abandoned. A free diuresis occurs in the babies of diabetic mothers—particularly in the large ones—resulting in a considerable loss of weight in the first few days

The mother's blood glucose concentration should be determined two or three hours after delivery—usually about midday—and, according to the result, an appropriate dose of soluble insulin should be given to cover the small meal which she should be able for in the afternoon. She is usually ready to take an adequate supper prior to which insulin may be given. On the following day her ordinary diet can often be tolerated Insulin requirements fall considerably after delivery, so that the dose of insulin should be drastically curtailed. Diabetic mothers should not be encouraged to nurse their babies as they seldom secrete sufficient milk, in consequence a suppressive dosage of œstrogens should be given and the daily diet reduced to that taken prior to pregnancy. Following discharge from hospital the patient should be seen at fortnightly intervals for a month or two to ensure that the diabetic control is satisfactory

Priscilla White's claim that the fœtal mortality in diabetic pregnancy can be greatly reduced by the administration of large doses of stilbœstrol during pregnancy has not been generally confirmed. it is probable that the excellent results obtained in her clinic are due more to the superb diabetic, obstetric and pædiatric management of her patients than to the hormonal therapy employed.

Diabetes *per se* does not constitute an indication for therapeutic abortion, though the presence of severe diabetic nephropathy or retinopathy may do so. Nevertheless, in respect of ultimate longevity, pregnancy constitutes a hazard to the diabetic mother and many authorities advocate sterilization after the second or third delivery—or earlier if the patient is no longer young and exhibits degenerative diabetic changes.

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It is therefore

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Should this contain more than 120 mg. per 100 ml. of glucose a full glucose tolerance test must be undertaken Even if this gives normal results it is wise to regard the patient as pre-diabetic and to keep her under careful observation from this point of view should she have a previous obstetric history suggestive of diabetes

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Even in the absence of obvious complications there is a considerable risk of intrauterine death of the child due to placental insufficiency and infarction. It is therefore important that the fœtal heart should be auscultated regularly and that the mother should report any diminution in fœtal movements. It is important to determine the size of the child, for it is wise to deliver by Cæsarean section the large or normal sized baby by the 35th or 36th week, whereas it is better to delay the operation in the case of a small baby as it is usually insufficiently mature to survive if delivered at this time, although this risk may be taken if the mother has a previous history of late intrauterine deaths. In any case, delivery should seldom be postponed beyond the 38th or 39th week. Each patient presents her own particular problems and the decision to operate should be the joint responsibility of obstetrician and physician. It is, however, not unusual for the mother to anticipate events by going into labour spontaneously. In such circumstances, in primiparous patients or in those with large babies, Cæsarean section should be undertaken as an emergency operation.

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account of late intrauterine deaths in previous pregnancies The most practical method is for the patient to take a breakfast containing 100 g. of carbohydrate at home (see p. 320) and to have a blood sample withdrawn two hours later. Should this contain more than 120 mg per 100 ml of glucose a full glucose tolerance test must be undertaken. Even if this gives normal results it is wise to regard the patient as pre-diabetic and to keep her under careful observation from this point of view should she have a previous obstetric history suggestive of diabetes.

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trophic and infective lesions. It is particularly important in regard to the healing *of wounds and the ability of the foot to stand daily weight-bearing.* The lack of pain often leads patients to delay coming for treatment until a slight infection in a corn or callus has extended and led to osteomyelitis. Thus trophic skin lesions and perforating ulcers like those of tabes occur in diabetic neuropathy, and are often confused by the inexperienced with gangrene. Trophic ulcers tend to heal more readily than gangrenous ulcers once the weight is taken off the foot, but they are frequently associated with peripheral vascular disease. Patients suffering from diabetic neuropathy should be given the same instructions regarding the care of the feet as those with peripheral vascular disease.

Diarrhœa is often a manifestation of a diabetic autonomic neuropathy and is characteristically nocturnal in nature and associated with tenesmus, urgency and sometimes incontinence. When diarrhœa occurs, the fat in the diet should be reduced and the fruit and vegetables and the coarse cereals should be omitted temporarily The carbohydrate should be increased by the addition of boiled milk, fine cereals and crisp toast. Symptoms of hypoglycæmia must be watched for in these cases. Codeine may prove helpful in doses of 30 mg. (½ gr.) and in severe cases 0 6 to 1 ml (10 to 15 min.) of tincture of opium may be given at night. A course of tetracycline treatment sometimes results in improvement.

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of the associated diabetes the management of such cases consists in drastic reduction of the sodium intake and the correction of the anæmia so often associated with renal failure.

The Adjustment of the Diet in Complications.—The average diabetic diet is unsuitable in cases of gastro-intestinal disturbances or in acute infections, since it is usually bulky and high in residue and may contain considerable amounts of fat and fried foods. No attempt must be made to force unsuitable standard diets upon a patient unable to digest or to enjoy them

The fluid feeds and the light diets given on pp. 319, 320, will be found suitable in many cases. It is impossible, however, to give detailed dietetic directions to suit all possible contingencies, and when diabetes is complicated by other diseases which make the standard diets unsuitable the practitioner will often be well advised to obtain the advice of a specialist.

FLUID FEEDS

(Each feed contains approximately 25 g. carbohydrate)

	CHO	*Prot.*	*Fat.*
Benger's Food, dry weight, ½ oz —15 g	12	1·5	0
Milk, 6 oz —180 ml	9	6	7
Sugar, 1 teaspoonful—5 g	5	0	0
	26	7·5	7
Orange juice, 3½ oz —100 ml	10	0	0
Glucose, ½ oz —15 g	15	0	0
Squeeze of lemon juice or lemon flavouring	..	.	
	25	0	0
Strained porridge, 4 tablespoonfuls	20	5	2
Milk, 3½ oz —100 ml.	5	3·3	4
	25	8·3	6
Bread, ¾ oz —22 g.	11	2	0
Milk, 6 oz —180 ml	9	6	7
Sugar, 1 teaspoonful—5 g	5	0	0
	25	8	7
Ovaltine, ⅓ oz.—10 g	7	1·5	1
Milk, 8 oz —240 ml	12	8	9·5
Sugar, 1 teaspoonful—5 g.	5	0	0
	24	9·5	10·5
Horlick's, ½ oz.—15 g.	11	3	1·5
Milk, 8 oz —240 ml.	12	8	9·5
Sugar, ½ teaspoonful—3 g.	3	0	0
	26	11	11

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Squeeze of lemon juice or lemon flavouring	.		. .
	25	0	0
Strained porridge, 4 tablespoonfuls	20	5	2
Milk, 3½ oz.—100 ml.	5	3 3	4
	25	8 3	6
Bread, ¾ oz —22 g	11	2	0
Milk, 6 oz —180 ml.	9	6	7
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Milk, 8 oz.—240 ml.	12	8	9 5
Sugar, ½ teaspoonful—3 g.	3	0	0
	26	11	11

Light Diabetic Diet

C. 162 g. P. 74 g. F. 87 g Cals. 1,727

Breakfast—

Strained porridge, 3 tablespoonfuls, or exchange (see p. 294).
Bread, 1 oz. (crisply toasted).
Diabetic marmalade, if desired.
Tea or coffee.
Milk and butter from allowance.

11 a.m.—

Glass of milk or white coffee made with milk from allowance. 1 tea biscuit.

Dinner—

Chicken, rabbit or any lean tender meat, 2 oz., or exchange (see p. 294).
Puréed vegetable, 1 tablespoonful.
Potato, 2½ oz.
Milk pudding made with ½ oz. cereal and milk from allowance.
Stewed apple, 3½ oz. *Or* orange, 3½ oz., or exchange (see p 295).

Tea—

Bread, 1½ oz., given as sandwich, if desired, using tomato, cress, lettuce or Marmite.
Tea.
Milk and butter from allowance.

Supper—

1 egg lightly cooked or exchange (see p. 294).
Bread, 1½ oz.
Tea
Milk and butter from allowance.

Daily—Butter or margarine, 1½ oz.; Milk, 1½ pints

The total calories of this diet are low and it is only suitable for temporary use.

In place of cereal pudding at dinner-time a milk soup may be given using 1 small teaspoonful flour
1 small teaspoonful margarine from allowance.
Milk from allowance.
1 tablespoonful puréed tomato, carrot or spinach.
Stock or Marmite may be added.
Or cereal may be omitted and ½ oz. bread added.

THE CARE OF THE SURGICAL DIABETIC

The discovery of insulin and the introduction of various anæsthetics as substitutes for chloroform and ether have greatly lessened the dangers of surgery in diabetic patients. Nevertheless, the risk of an operation is still considerable if the patient falls into inexperienced hands Successful treatment depends upon close co-operation between the surgeon and the physician, and, if possible, a nurse who is experienced in the care of diabetic patients should be employed.

The risks involved are those of ketosis on the one hand and of hypoglycæmia on the other Ketosis may result from the administration of an unsuitable [illegible]

It has been shown that the use of ganglion blocking agents in diabetic patients may result in marked hypoglycæmia, and such agents should not, therefore, be employed when insulin is being used

The routine measure of testing every patient's urine before operation is an obvious necessity, since it may be too late to give adequate treatment if the diabetes is only discovered after the operation.

It is impracticable to outline a routine to be followed for all patients with diabetes. Experience is the only sure guide to treatment. The method of preparing the patient will vary according to whether the operation is undertaken as an emergency measure or whether the patient can be prepared for surgery at leisure. Furthermore, the treatment must be modified to suit the surgical condition

Elective Surgery.—Whenever possible the patient should be admitted to hospital several days before the operation for stabilisation of his diabetes. A [illegible]

during the pre-operative period and to ensure the metabolism of this substance [illegible]

has previously been accustomed

When a prolonged surgical operation is to be performed—particularly when post-operative feeding is likely to be uncertain—intravenous glucose must be given with a suitable dose of insulin in order to prevent starvation ketosis An infusion of isotonic glucose is started two hours prior to the operation and maintained until carbohydrate can be taken orally. The dose of insulin is determined by frequent blood glucose estimations The first dose is given when the infusion is started . in a patient suffering from mild diabetes not previously requiring insulin, 12 units of soluble insulin should be sufficient ; 16 units is a fairly com [illegible]
of insulin [illegible]
than depo [illegible]
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ketosis [illegible]

It has been the previous practice to give the patient oral carbohydrate in the form of glucose or Benger's Food four to six hours pre-operatively, with an estimated dose of soluble insulin Experience has shown, however, that such [illegible]

consequent aspiration pneumonia It is now customary, therefore, to give the patient his normal diet and insulin on the day *before operation, which is timed* for mid-morning; breakfast is withheld and the blood glucose concentration is determined two hours before the administration of the anæsthetic. If this is found to be less than 100 mg. per 100 ml., an appropriate amount of hypertonic glucose is given as a single intravenous injection, whereas if the blood glucose is in excess of 220 mg. per 100 ml. a suitable dose of soluble insulin is administered. Between these extremes no pre-operative treatment with insulin or glucose is usually required and the blood glucose concentration, estimated at frequent intervals during and immediately after the operation, does not deviate significantly from the pre-operative level. Moreover, provided the patient is able to eat within a reasonable period after the operation, starvation ketosis does not develop.

During the immediate post-operative period patients in whom there is some contra-indication to oral feeding and patients in whom vomiting occurs will

Patients who have undergone less serious surgical procedures are usually able to take carbohydrate by mouth a few hours after operation. If this takes place in the morning the patient may feel inclined for a cup of tea with a lump of sugar (5 g.) in the late afternoon. In the evening a fluid feed of 25 g. of carbohydrate (see p. 319) can usually be taken This is preceded by soluble insulin in

remembered that during the post-operative period the requirement for insulin is often increased Apart from the hyperglycæmia which occurs after a general anæsthetic the nervous shock which is inevitable in any operation tends to raise the blood glucose concentration. Moreover, in the presence of sepsis carbohydrate tolerance is still further diminished. As the patient recovers the improvement in sugar tolerance is often striking and care should be taken to ensure that hypoglycæmia does not occur at this stage.

glycosuria is present. If the usual diet can be taken after operation, a patient having insulin should receive his customary dose.

The diet for a case of cataract must be served in such a form that little mastication is necessary until the patient is discharged from hospital. It is

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Fluid Diet

For temporary use only

C. 145 g. P. 40 g. F. 50 g. Cals. 1,190

Early morning—
Cup of tea with milk from allowance.

Breakfast—
Strained porridge, 5 tablespoonfuls.
Hot milk, 5 oz. from allowance.

10.30 *a m* —
Glass of milk from allowance.

Dinner—
Milk Soup .
1 small teaspoonful of flour
1 small teaspoonful of margarine.
1 tablespoonful of puréed carrot or spinach or tomato.
Milk, 5 oz from allowance.
Seasoning.
Stock or Bovril as required.
Stewed apple, 3½ oz , or other fruit—see list.

**Tea*—
1 thin slice of bread with butter, ¼ oz , or 2 tea biscuits
Tea with milk from allowance.

Supper—
Benger's Food, ½ oz.
Milk, 7 oz. from allowance.
Lactose or sugar, 2 teaspoonfuls, ¼ oz.

9 0 *p.m.*—
Orange juice, 3 oz.
Lactose or sugar, ¼ oz
Dilute with water.
or Milk, 7 oz. extra to allowance.
Horlick's or Ovaltine, ½ oz.

Total milk allowance—1½ pints.

* If patient is unable to take bread or biscuit, give as soft bread and milk *or* 3 oz. orange juice+¼ oz. lactose or sugar.

OBESITY

INTRODUCTION

Up to the beginning of this century corpulence was on the whole regarded as a desirable and healthy attribute, and it has only been comparatively recently that medical interest has been focused on the more serious aspects of excessive weight. *Quite apart from æsthetic considerations, long-continued obesity has* as its almost invariable concomitants more or less grave disturbances of most of the systems of the body. Thus the statistics of Life Assurance Companies all go to show that mortality rates rise steadily in proportion to the extent to which people are overweight. It seems that a man 50 lb overweight at the age of forty-five has no better expectancy of life than the average expectancy for all forms of valvular heart disase Flat foot, varicose veins, osteo-arthritis of the knees and hips, postural backache, ventral herniæ, cholecystitis and gall-stones, diabetes, degenerative changes in and overstrain of the myocardium, angina pectoris, hypertension, bronchitis, and post-operative pulmonary complications

reduction in weight is sometimes the only treatment required to banish the symptoms arising from the milder forms of such conditions

and food intake. The glutton does not necessarily become overweight, nor is the ascetic necessarily emaciated. It is certain that most of us eat in excess of

ments, such as would be represented by an extra glass of milk or two slices of bread, would have the result of increasing the weight by some 24 lb. a year; an

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the body some fundamental mechanism for conserving or eliminating surplus energy of which we are as yet in almost complete ignorance. Overeating may have both a physical and psychological basis, and it is probable that appetite is normally controlled by the hypothalamus—that mysterious region in the brain where psyche and soma meet. Experimental lesions in this area of the brain stem result in voracious appetite in animals, so that they become excessively obese. A counterpart in man is to be seen in the obesity which characterizes

It is commonly believed that obesity is usually the result of endocrine disturbances, particularly failure of the anterior pituitary Actually endocrine disease is seldom the cause of obesity, and failure of the anterior pituitary is more

often characterized by cachexia than by obesity. The anterior pituitary may be involved in the obesity which so often characterizes diabetes, but whatever part the pituitary plays in this respect it is in the direction of *over-* rather than *under-*activity. Another common error is to believe that the thyroid is at fault, for obesity is by no means an essential feature of myxœdema. It is true that patients suffering from Cushing's syndrome and certain types of eunuchoidism are frequently very fat, but these are rare disorders and on the whole there are no good grounds for blaming the endocrine glands in most cases of obesity.

In every case of obesity income exceeds expenditure, and rational therapy must consist in correcting the balance. However we may try to escape from it, we are eventually confronted with the fundamental law that matter cannot be created or destroyed. Nobody can make fat out of nothing, and fat can only

owing to the disabling effects of obesity it is rarely possible for a fat person to take really hard physical exercise The alternative to exercise is to employ hormone or drug therapy to influence the activity of tissue metabolism Drastic purgation by hypertonic salt solutions and the encouragement of profuse sweating by Turkish baths have had, and still have, their vogue as treatments of obesity.

especially

effects—tl

almost entirely due to a temporary loss of water from the body. The only practical procedure, therefore, in the treatment of obesity is dietetic restriction, using rationally constructed subcaloric diets

DIETETICS

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exceed 25 Cals per kilogram of the standard body-weight, which represents the requirement of the healthy individual under basal conditions. In practical

prescription of a diet of 1,000 or 1,200 Cals. is all that is necessary. Occasionally, a *hard-working man may require one of 1,500 Cals, but it must be*

patients who are not confined to bed. They are seldom adhered to, and if they are observed in the letter they cause weakness, faintness and an unduly rapid loss in weight. Very low calorie diets may be employed, however, in resistant cases under observation in hospital.

IDEAL WEIGHTS FOR WOMEN. AGES 25 AND OVER

Height (*with shoes*)		Weight (*as ordinarily dressed*)		
		Small Frame	*Medium Frame*	*Large Frame*
ft.	in.	st. lb. — st. lb.	st. lb. — st. lb.	st. lb. — st. lb.
4	11	7 6 — 7 13	7 12 — 8 6	8 5 — 9 1
5	0	7 7 — 8 1	8 0 — 8 8	8 7 — 9 3
5	1	7 9 — 8 3	8 2 — 8 10	8 9 — 9 5
5	2	7 12 — 8 6	8 5 — 8 13	8 12 — 9 9
5	3	8 1 — 8 9	8 8 — 9 2	9 1 — 9 12
5	4	8 4 — 8 13	8 12 — 9 6	9 5 — 10 2
5	5	8 7 — 9 2	9 1 — 9 9	9 7 — 10 5
5	6	8 11 — 9 6	9 4 — 10 0	9 12 — 10 10
5	7	9 0 — 9 10	9 8 — 10 4	10 2 — 11 0
5	8	9 3 — 9 13	9 11 — 10 7	10 5 — 11 4
5	9	9 7 — 10 3	10 1 — 10 11	10 9 — 11 8
5	10	9 10 — 10 7	10 5 — 11 1	10 12 — 11 12
5	11	9 13 — 10 10	10 8 — 11 4	11 1 — 12 1

METROPOLITAN LIFE INSURANCE COMPANY, Statistical Bureau, 1943.

IDEAL WEIGHTS FOR MEN. AGES 25 AND OVER

Height (*with shoes*)		Weight (*as ordinarily dressed*)		
		Small Frame	*Medium Frame*	*Large Frame*
ft.	in.	st. lb. — st. lb.	st. lb. — st. lb.	st. lb. — st. lb.
5	2	8 4 — 8 13	8 12 — 9 7	9 5 — 10 2
5	3	8 7 — 9 2	9 1 — 9 10	9 7 — 10 4
5	4	8 10 — 9 6	9 4 — 10 0	9 11 — 10 9
5	5	9 0 — 9 10	9 8 — 10 4	10 1 — 10 13
5	6	9 3 — 9 13	9 11 — 10 7	10 5 — 11 3
5	7	9 7 — 10 3	10 1 — 10 11	10 9 — 11 8
5	8	9 10 — 10 7	10 5 — 11 2	10 13 — 11 12
5	9	10 0 — 10 11	10 9 — 11 6	11 3 — 12 2
5	10	10 4 — 11 1	10 13 — 11 10	11 7 — 12 7
5	11	10 8 — 11 5	11 3 — 12 0	11 11 — 12 12
6	0	10 12 — 11 10	11 7 — 12 5	12 1 — 13 3
6	1	11 3 — 12 1	11 12 — 12 10	12 6 — 13 8
6	2	11 9 — 12 7	12 3 — 13 2	12 11 — 14 0
6	3	12 0 — 12 12	12 8 — 13 7	13 2 — 14 6

METROPOLITAN LIFE INSURANCE COMPANY, Statistical Bureau, 1943.

This *extreme* reduction of fat makes the diet difficult and unpalatable, and is therefore undesirable. The diets given below contain from 40 to 50 g of fat.

Carbohydrate.—Since excess carbohydrate eating is the most important single ætiological factor in obesity, the carbohydrate should be restricted as far as possible in obesity diets Sufficient carbohydrate, however, must be given

ful sparers of protein, and their too severe restriction leads to excessive loss of

satiety and at the same time of providing roughage to combat the constipation which subcaloric diets always tend to produce.

Protein.—Because of its specific dynamic action on metabolism, protein was often given in large quantities in reducing diets (*e g.* Banting and Salisbury diets); but as this means a higher caloric intake its advantage is somewhat doubtful, and such diets are ill-balanced, expensive and impracticable. If, on the other hand, the protein of the diet is too low, a negative nitrogen balance will result from excessive destruction of tissue protein. The optimum intake of protein for a subcaloric diet should vary from about 60 to 80 g. per day

Salt.—Apart from alcohol and sweetened drinks, no attempt need be made to restrict fluids, but the intake of sodium chloride should be curtailed. Salty foods should be avoided and as little table salt as possible should be taken In some cases of obesity, retention of salt and water may be a very important factor. Accordingly the administration of mersalyl by injection or ammonium chloride by mouth may be valuable as a temporary expedient.

Obesity Diets

Notes.—The following notes apply to all the sample obesity diets given :

The helpings of food are expressed in ounces instead of in grammes, since a reducing diet is most often used in the patient's home. If weighing on gramme scales, 1 oz. may be reckoned as 30 g

Bread and butter should be weighed and milk must be measured It is convenient to measure the butter and milk in the morning and use them as

white.

Salt is to be taken in moderation.

Foods to be avoided.

Sugar, sweets, chocolate, jam.
Scones, cakes, pastry, cereals.
Thick soups and sauces made with flour or butter.
Fried foods, cream and salad dressings.
Pork, duck, goose, fat meat and bacon.
Sweet wines, beer, stout, spirits or sweet aerated water.
Nuts

Fruits—
Dried, canned in syrup, bananas.
Grapes and plums allowed in moderation only.

Vegetables—
Potato, dried or fresh peas, dried beans, parsnips.
Beetroot allowed in small quantities only.

Foods with no appreciable Caloric Value.

Oxo, Bovril, Marmite, clear soups. (Avoid excess of meat extracts because of their salt content)
A dessertspoonful of sugarless marmalade or jam (as sold for diabetics).
Gelatin, egg-white, green vegetables, vinegar, tea, coffee, unsweetened pickles.

Obesity Diet

Carbohydrate, 100 g.
Protein, 60 g. (approximate daily average)
Fat, 50 g. (approximate daily average).
Calories, 1,100.

Breakfast—

*Orange or ½ grapefruit without sugar.
Bread, 1 oz. (1 thin slice), *or* 2 pieces of Ryvita or Vita-weat.
Butter from ration.
1 egg, *or* 1 oz. *lean* cold boiled ham or tongue or grilled sausage, *or* average helping of finnan haddock.
Tea *or* coffee with milk from ration.

Dinner—

[illegible] or Bovril, if desired
[illegible] cooked *lean* meat, chicken, rabbit, tripe
[illegible] ¼ oz. butter may be used for cooking.)
A large helping of vegetables, preferably from Group I (see p 295). as often as possible.
*1 apple, or pear, or other fruit. (See p. 295).

Tea—

(Now or at supper)—1 egg, *or* ¾ oz. cheese, *or* medium helping of white fish, lean meat, chicken, *or* 1 oz. cooked lean ham or tongue.
Fresh salad or tomato.
Bread, 1 oz.
Butter from ration.
Tea or coffee with milk from ration

* One helping of fruit can be replaced by ½ oz. of extra bread or two water biscuits, which give approximately the same number of calories.

Supper—

Bread, 1 oz.; *or* 2 pieces of Ryvita or Vita-weat, *or* 3 water biscuits.
Butter from ration.
Milk from ration; coffee, if desired.
*1 medium-sized orange, or choice from the list.

Rations for Day—

Butter, ¾ oz. Milk, ½ pint

No sugar. Saccharin or Saxin can be used.
Water, 4 glasses, preferably not with meals.

To increase this diet to 1,220 Cals. add 1 oz. bread and ¼ oz. butter.
To increase to 1,450 Cals add 2 oz bread, ¼ oz. butter, and 1 oz. meat or exchange (see p 294).

EXPENSIVE OBESITY DIET

This diet allows for greater variety than the other. It includes more expensive foods and has a higher protein content.

Carbohydrate, 100 g
Protein, 84 g (approximate daily average).
Fat, 52 g (approximate daily average).
Calories, 1,204.

Breakfast—

Fresh peach, slice of melon, ½ grapefruit or orange.
1 egg; *or* 1 oz. cold lean ham or tongue. (If preferred, use the egg for custard or serve as a savoury at dinner.)
Ryvita or Vita-weat, 2 pieces; *or* bread (preferably brown), 1 oz. (1 thin slice).
Butter, 2 small balls, ¼ oz., from ration.
Tea or coffee with milk from ration.

Lunch—

Tomato juice cocktail, if desired.
Meat: Medium-sized helping of cooked *lean* meat (2 to 3 oz.), or chicken, or game, or white fish—a good-sized fillet, grilled or baked with ¼ oz. extra butter
Or [illegible]

Or
Ve
etc. Vegetable, as desired.
Fruit, 1 apple or pear or other fruit (see p. 295)
Cheese, one section ¾ oz
Ryvita or Vita-weat, 2 pieces; *or* 3 water biscuits.
Coffee, if desired, with milk from ration

4 p m.—

Tea, if desired, with milk from ration

* If unavailable, fruit can be replaced by ½ oz. of extra bread or two water biscuits, which give approximately the same number of calories.

Dinner—

Clear soup, if desired.

*Fish : Fillet of sole (approximately 2½ oz.) grilled with butter from ration *Or* lobster or crayfish. Salad as desired.
Or 1 doz. oysters—lemon juice.

*Meat · Noisettes of mutton (centre of 2 grilled cutlets=2 oz. meat).
Or chicken, game or braised sweetbread.

Vegetable as desired.

Fresh fruit as before.

Ryvita, 1 piece ; *or* ½ slice thin toast.

Milk from ration can be used for curds, milk jelly, custard (using egg from breakfast, or omitting fish) ; or sauce can be made with butter from allowance and 1 teaspoonful of flour (omitting Ryvita, 1 piece) Flavour with vinegar, lemon juice, tomato purée, anchovy essence, parsley mushroom or a few oysters.

Rations for Day—

Milk, ½ pint. Butter, ¾ oz.
No sugar. Saxin or saccharin, if desired.

To increase this diet add extra butter, which will greatly add to the palatability. Each ½ oz. butter=112 Cals.

DRUGS

Thyroid.—The well-known stimulating effects of thyroid on metabolism have been utilized in the treatment of obesity since the end of the nineteenth century. Its popularity has waxed and waned. The modern view is that, unless true subthyroidism is present, it should seldom if ever be used. Given in ordinary doses of 0 2 g. (3 gr) a day to obese patients with a normal thyroid [illegible] that the normal person is less sensitive to the action of administered thyroid than the myxœdematous patient. Large doses—sufficient to produce a degree of hyperthyroidism—will cause loss of weight, but may also cause tremor, nervousness, diarrhœa, palpitation and tachycardia. Such induced hyperthyroidism is peculiarly ill-borne by obese patients whose hearts are often fatty and overstrained.

Amphetamine.—Amphetamine sulphate, by depressing the appetite, [illegible]

which may be experienced by patients eating restricted diets The drug is [illegible]

so they may be unable to tolerate amphetamine, even in the small doses suggested,

* If both fish and meat are not desired, a large helping of either could be taken, e g., 2 fillets of fish or ¼ lb grilled fillet steak.
If fish only is taken, ¼ oz extra butter may be allowed for cooking.

without experiencing palpitation, tremor and nervousness. It is a vasocon-

THE CONTROL OF TREATMENT

Patients undergoing reduction in weight should be seen frequently by the doctor. Their dietetic enthusiasm tends to wane unless they receive constant

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become careless about their diet when they go on holiday, or may be unable to observe it accurately in hotels or lodgings. The labour of months may be undone in this way in a few weeks We have known, for example, one patient who regained 7 lb. during the course of a week's holiday, and this is not an exceptional case.

Patients should be weighed weekly, and an average loss of between 2 and 3 lb. a week should be aimed at If the weight loss is constantly more rapid than this, the diet should be slightly increased When the loss, on the other hand, does not average 2 lb a week, the patient should be carefully questioned as regards her strict observance of the diet, as slackness in this respect is far the most common cause of failure to lose weight satisfactorily. Occasionally, however, it may be necessary in such cases to modify the diet still further from perhaps 1,200 to 1,000 Cals.

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ascertain the real rate of loss over short periods and make it unnecessary to weigh the patient more than once a week Some of these fluctuations may depend on whether or not urine or fæces have been evacuated before weighing, but changes in water balance probably account for most of them. In addition to these daily variations a disturbance in weight loss often accompanies menstruation For two or three days before the period weight loss usually ceases, and a slight gain may occur, to be followed about the middle of the period by an increased rate of loss.

It may be said that with rare exceptions all patients who keep to the régime outlined above lose weight satisfactorily, though they vary considerably in the rate at which this occurs. Thus, those who are initially grossly overweight lose on the average more rapidly than those in whom the initial excess weight is only moderate. The response to treatment is very comparable in those who have been

. Long-

there is often a tendency for corpulence to return when treatment is entirely discontinued. Usually a slightly modified normal diet is sufficient to counteract

this tendency. The patients have learned dietetic discretion and are generally able to maintain their weight at the new low level by the exercise of a little care, so that very strict dieting is no longer necessary. In a few unfortunate people, however, the slightest relaxation in dietetic care is followed by a rapid gain in weight. This occurs particularly in those who were originally grossly obese and who have lost weight rapidly under treatment. Indeed, the greater the original obesity and the greater the response to treatment, the greater must be the care in relaxing treatment.

No attempt should be made to reduce a very fat woman to the "ideal" weight for her height and age, given on p. 326, nor should girls in search of a fashionable figure be allowed to reduce themselves to unduly exiguous proportions. The practitioner must use his common sense in these respects.

In conclusion, it may be said that there are few therapeutic measures in medicine so certain to produce results as the prescription of a subcaloric diet to an obese patient, provided there is strict adherence to the prescribed diet. In addition, there are few purely medical measures so likely to restore health or to prevent disability as the controlled weight reduction of obese persons. Like so many other forms of therapy, however, much harm can be done by excessive enthusiasm, by an attempt to produce in a few weeks a result which should only be attained in many months, or by trying to slim people of already normal proportions. It must also be remembered that there is no royal road, nor even a short-cut, along which an obese person may travel safely to an ideal weight, but only along the thorny path of dietetic restriction, for little reliance should be placed on drugs in the treatment of obesity.

D. M. DUNLOP.

NUTRITIONAL DISORDERS

By definition, nutritional disorders are those which are due to faulty diet: the patient has received too much or too little food, or not enough of the right kind. Too much food results in obesity, discussed on p. 324. Simple lack of food is now an uncommon cause of ill-health in Great Britain. Yet for mankind as a whole, deficiency of calories is far more important as a cause of ill-health than all the vitamin deficiencies put together. The population of the world is steadily increasing through the expanding application of medical science; but the application of agricultural science has failed to keep pace with it. Consequently, today at least one-third of humanity is not getting enough to eat.

Even in countries where the total supplies of food are sufficient, nutritional disorders may arise through poverty, ignorance or bad housekeeping aggravated by bad housing. The children of large families living in industrial cities or on impoverished farm-land, and the old and solitary dependent on their own resources, are most frequently affected

interfering with the absorption, digestion or utilization of their food, or by increasing their nutritional requirements so that their usual diet becomes insufficient.

CALORIES

Requirements.—The quantity of food necessary to provide an individual person with sufficient calories cannot be predicted from published tables of "requirements". Energy expenditure varies enormously from one individual to another, even among people of the same age, sex, size and habits In fact, tables like those published by the British Medical Association (1950) are not intended to express *requirements*, they are "recommended allowances", providing standards against which to judge the adequacy of the food consumed by groups of people such as the population of a school, a city or an entire

energy value of the food actually eaten Food administrators more often deal with "retail" calories the value of the food at the time that it is sold in the shops. No comparison between retail calories and recommended allowances can be made without some deduction for wastage

Subnutrition (Underfeeding)—Calorie Deficiency.—The prolonged consumption of too little food results in loss of weight in adults and restricted growth in children. It is not always easy to diagnose subnutrition on simple clinical inspection; some people are thin by nature, though in excellent nutritional health But repeated measurements showing loss of weight or failure to grow provide important evidence of subnutrition One of the most useful things that a doctor can do towards keeping his patients in health is to weigh them regularly The appearance of loose folds of skin may also give evidence of recent loss of weight People partly adapt themselves to an insufficient caloric intake by restricting unessential bodily movements, consequently the behaviour of children in a school playground may tell more about their state of nutrition than a medical examination.

A good example of conditioned subnutrition is provided by the thin diabetic whose fall in weight is due to loss of calories in the form of sugar in the urine Conditioned subnutrition may also arise as a result of any gastro-intestinal disorder that sufficiently impairs appetite or interferes with digestion Prolonged fevers raise the metabolic rate and so increase the need for calories; but the patient may be disinclined to eat, and so develops subnutrition, this is especially true if the patient is a child, who should be actively growing. A clinical state

countries now have well-developed Maternity and Child Welfare Services, through which milk and school meals are supplied Full use should always be made of such services in the treatment of underfed children Similarly, the

" meals on wheels " scheme, run by *the Women's Voluntary Service in Britain*, for delivering hot, ready-cooked meals to old people living by themselves, is an invaluable service for maintaining the nutrition of this " vulnerable group " and keeping them out of hospital. Where subnutrition arises as a direct result of poverty, the physician should make certain that full advantage is taken of any existing organizations—local, national or charitable—for financial assistance When the chief fault lies in the disorganized feeding arrangements of a slum home, the local housing authority can sometimes help, and the doctor should approach the medical officer of health Simple parental ignorance or neglect may sometimes result in children being given unsuitable food; in such cases the physician, aided by the health visitor, must educate and admonish. The single, most important therapeutic means of combating nutritional disorders of all *kinds is good cooking, the art of a good cook is of more value than any number* of " tonics " or other supposed stimulants to appetite. The physician should ensure that his patients receive appetizing food, both at home and in hospital.

The Use of " Appetizers ".—Tonic mixtures containing gentian or other bitters have a long tradition as appetizers to encourage the underfed patient to eat. Lately they have tended to be supplanted by vitamin B_1 (thiamine, aneurine), either alone or combined in a variety of proprietary mixtures. This vitamin has been thought to be good for appetite because animals deprived of it suffer from anorexia. But anorexia is not especially pronounced in human

Starvation.*—Starvation may conveniently be defined as subnutrition of* sufficient severity to require in-patient treatment in hospital. The starving patient is emaciated, having lost 25 per cent. or more of his original weight. His eyes are dull and the whiteness of the scleræ unusually vivid; his hair is dry and inflexible (" staring hair "), his skin is thin, dry, inelastic, often splotched with dirty brown pigmentation, and his extremities are cold and cyanotic even

total body water is not reduced, so that with the wasting of tissues, œdema ultimately appears, not necessarily associated with any reduction in plasma protein concentration. The œdema is usually most obvious in the face and lower limbs. The number of circulating red blood corpuscles diminishes, without much change in plasma volume; the result is a moderate anæmia, *usually normocytic and normochromic.*

The agricultural, political or social conditions that created this desperate condition must be overcome—if possible. The patient should be removed to an entirely fresh environment, with good nursing and a new hope in life. If the cause is a famine, he should be transferred to an emergency hospital as near as possible to his home. Starving people do not readily recover without new hope.

Food is obviously the next consideration, but what food? Many starving people have died because they were given anything that well-meaning relief workers happened to have available: tins of bully-beef, baked beans or brown bread. Diarrhœa, from eating unsuitable food, may result in dehydration and death.

In starvation the single most important therapeutic agent *is skimmed milk*

(fresh or dried). In times of famine its supply should be controlled by the medical officer and it should be distributed as a medicine. Frequent small feeds, as often and as much as the patient will tolerate, are required; this demands vigilant nursing care. The appetite is usually fickle and may be completely absent. Variation of flavour—vanilla, chocolate or strawberry—may help to stimulate it; but curiously, there is often a dislike for sweet things; sour curds (yoghourt) may be more successful. The paper-thin walls of the wasted intestines are intolerant to coarse foods and the lack of digestive juices impairs, particularly, the absorption of fats, therefore the cream of the milk is best excluded. Predigested (hydrolysed) protein by mouth has no apparent advantage over skimmed milk, except that its strong flavour may temporarily stimulate appetite.

There comes a point in severe starvation when the patient, though still fully rational, refuses all food. The prognosis then is very grave, despite the best of care; a slow nasal drip of skimmed milk should be tried, but at subsequent autopsy the milk may be found lying in the stomach.

Parenteral feeding is usually of little help and has dangers The small brown-atrophied heart does not readily tolerate any additional load, which may precipitate pulmonary œdema If adequate supervision is possible, half a litre of normal-strength plasma by slow intravenous transfusion may be tried in selected cases, though if famine œdema is present, it may draw additional fluid from the tissue-spaces and place a further burden on the heart. Hydrolysed protein for intravenous use is best avoided.

[illegible]

rapid re-feeding should be checked, even when the patient begins to walk. Further details about dietetic treatment are given on p. 338, under nutritional œdema. Recovery may take many months, but is usually complete provided there are no complications, such as tuberculosis, which is a frequent aftermath of famine.

Though specific vitamin deficiency disorders are rare in Europe, they are common among people surviving on meagre rations of rice or maize, and may give rise to permanent disabilities later. Infections of various kinds are common [illegible]

[illegible]

depression and apathy. The physician must tolerate this with sympathy and must not expect thanks for his efforts

MALNUTRITION
(DISORDERS DUE TO QUANTITATIVE DIETARY DEFICIENCIES)

It is suggested that the term "malnutrition" should be restricted to those nutritional disorders which are due to an insufficient consumption of particular

nutrients: specific chemical substances such as amino acids, minerals or vitamins. In this way the qualitative aspects of faulty nutrition will not be confused with the quantitative. Malnutrition and subnutrition (underfeeding) frequently coexist, but by no means always.

The Components of an Adequate Diet.—*Carbohydrates and Fats.*—Though carbohydrates provide the greatest part of the calories in most normal diets, no single carbohydrate is indispensable to health, in the sense that the body has a special metabolic use for it and cannot make it from other nutrients. Fats have a high caloric value and are extremely useful in good cooking. They are therefore important in making a diet appetizing and small in bulk. A patient on a liberal allowance of fat is better off than one whose belly is " crammed with distressful bread " ; nevertheless, it has yet to be shown that fats in themselves have indispensable chemical virtues for the maintenance of satisfactory nutritional health. Claims that unsaturated fatty acids are needed to prevent certain skin disorders are not supported by reliable scientific evidence.

Proteins and Amino Acids.—The proteins of food are the only important source of nitrogen, sulphur and essential amino acids. An adequate diet must contain sufficient protein to satisfy the body's need for these essentials. There must be enough to maintain a positive nitrogen balance, so that the nitrogen lost in the urine is replaced Of the twenty-three known amino acids, only ten seem to be " essential " for man, in the sense that the human body is incapable of making them for itself and must obtain them from food. These ten are: lysine, tryptophan, phenylalanine, leucine, isoleucine, threonine, methionine, valine and (probably) histidine and arginine. Their names are given here because some of them are now available in synthetic form and may prove to have therapeutic uses. Although little is yet known of the metabolic role of most of them, they may have a place in the food strategy that is so important in times of war and other national emergencies Further, if they can be manufactured at economic prices they may some day be offered direct to the public—even to the overfed public—to supersede self-medication with vitamins.

The remaining " non-essential " amino acids, which the body makes for itself when given an adequate supply of the others, are nevertheless important

ide nitrogen One of them,
e only source of sulphur in
meaty taste that has given
it a marketable value as a flavouring agent.

Some proteins are notably deficient in certain amino acids; e.g. zein, the chief protein of maize, contains no lysine or tryptophan; gelatin contains no tryptophan, valine or methionine. On the whole, individual animal proteins have better " biological value " than plant proteins, in that they supply a more varied mixture of amino acids. This has been used to argue the need for abundant meat (by those who enjoy their beef steaks)—an argument that did much to lose the 1914-18 war for the Germans, who used their limited land to raise beef rather than bread Though some animal protein is certainly desirable and probably essential, there is good evidence that satisfactory nutrition

supplied by another.

Whether a diet is adequate in protein is generally best decided by calculating

the contribution that the proteins make to the total calories consumed A satisfactory diet for a healthy person should contain sufficient protein to provide not less than 11 per cent of the total calories, or 14 per cent in the case of a lactating woman. When, for any reason, the diet is restricted in calories, this general rule may break down; the daily intake of protein for an adult should not be less than 50 g. There is no evidence that hard physical work increases the rate of utilization of protein.

Water and Minerals.—The effects of water and salt (sodium chloride) deficiency are discussed on p 105. Of the other mineral elements present in the human body and known to have physiological activity, potassium, magnesium, manganese, zinc, copper and cobalt are apparently never lacking in natural diets. Iron deficiency is a very common cause of ill-health among women in Britain during their menstrual life, it is discussed on p. 402 Nutritional needs for sulphur are supplied by the sulphur-containing amino acids (p. 510). Provided that a diet contains sufficient calcium, it will normally provide sufficient phosphorus; deficiency of calcium is inseparably connected with the problem of rickets and osteomalacia (p 341). Iodine deficiency is discussed in relation to simple goitre (see p. 351).

Fluorine is of interest in connection with dental caries. If the drinking

caries, probably because of the bacteriostatic properties of fluorine which is deposited in the enamel In many cities in America fluorine is now deliberately added to the water supply, to the extent of 1 p.p m., as a prophylactic measure against caries It should be remembered, however, that fluorine in excessive amounts is toxic, producing a form of spondylitis and other changes in bone.

Vitamins.—Laboratory workers have discovered and described many vitamins in recent years, but only nine are unquestionably important in human nutrition. These are.

Fat-soluble:

Vitamins A, D and K.

Water-soluble:

Ascorbic acid (vitamin C) and five components of the vitamin B complex: thiamine (aneurine), nicotinic acid (niacin), riboflavin, folic acid and cyanocobalamin.

Vitamin K deficiency is conditioned by biliary obstruction; it is discussed on p. 442. The parts played by folic acid and vitamin B_{12} in hæmopoiesis are discussed on pp 414-16.

The therapeutic uses of vitamins A, D and C, thiamine, nicotinic acid and riboflavin will now be discussed in relation to specific nutritional disorders.

Three other components of the vitamin B complex have been reported to have therapeutic effects: pantothenic acid (see p 347 under "burning foot" syndrome), pyridoxine (see p. 341 under angular stomatitis) and biotin. The only known case of human biotin deficiency was that of a man who had subsisted on an extraordinary diet of raw eggs and red wine.

Fat-soluble vitamin E occurs in human tissues and has interesting biological properties as an anti-oxidant; but there is no indisputable evidence that ordinary mixed diets are ever deficient in vitamin E or that it has any therapeutic application (see p 349).

Nutritional Œdema.—There are at least four possible dietary causes of œdema which should be distinguished:

Beriberi, with or without cardiac failure (see p. 346).

Famine Œdema.—The iso-hydric type already described (p. 334), in which œdema appears in starving people through wasting of tissues without any change in the volume of body water; *the level of plasma proteins may be within normal limits.*

Famine Œdema associated with protein deficiency, in which the plasma proteins are reduced, and the consequent reduction in osmotic pressure of the plasma contributes to the œdema.

Until recently it was thought that famine œdema was due solely to this reduction in the osmotic action of the plasma proteins, but it is now realized that wasting of tissues has also an important part to play in its production. Experience shows that famine œdema is likely to arise whenever people subsist for long periods on a diet providing less than 1,000 Cals. and less than 50 g of protein daily The œdema is usually most evident in the face if the patient has been lying down. But when the patient gets up and walks about, it shifts quite rapidly to the feet and legs. It may be so extensive as to conceal the underlying emaciation.

value, such as junket, curds, custard made from milk and eggs, pounded fish, minced lean meat or chicken. It is important that the diet should also contain adequate carbohydrate to "spare" the proteins, so that they are used to replenish

Milk

In the

g with

ordinary foods, cooked with salt, may increase the œdema. Restriction of

to see that the diet remains well-balanced, providing adequate amounts of the "protective foods," particularly dairy produce, meat, fruit and vegetables A sudden increase in the caloric intake of an underfed patient, as for instance by an increased ration of polished rice or by large amounts of glucose given by mouth or vein, may precipitate an acute state of vitamin depletion (see p. 339 under beriberi).

Conditioned protein depletion occurs in the nephrotic syndrome (p 708) and sometimes in cirrhosis of the liver (p. 511)

Epidemic Dropsy.—Epidemics of this disease have claimed many victims in

Careful research by Indian workers has traced its cause to a toxic substance that has been isolated in crystalline form from the seeds of the Mexican Poppy, *Argemone mexicana*, sometimes erroneously and libellously called "Scotch thistle". Seeds of this weed find their way, by accident or design, into mustard seed from which cooking oil is extracted. They may also contaminate bread grains. Treatment obviously consists in withdrawing the contaminated food. There is no known specific antidote

Diseases due to too much Dependence on Cereals.—The cultivation of [illegible] develop.

Cereals in general have certain qualitative defects as "the staff of life". Their protein is poor in some essential amino acids, and though the germ and [illegible] unavailable because of their insoluble combination with phytic acid, which is present particularly in the outer layers of the grain Because of this, it is advisable that calcium carbonate should be added to flour by the millers in amounts sufficient to neutralize the phytic acid

Fortunately for the Scots (and for horses in England), oats are superior to all other grains in nutritive value, except for their high phytic acid content; the traditional habit of taking porridge with milk (rich in calcium) corrects this one defect.

Cardiovascular (wet) Beriberi.—This disease is practically confined to rice-eaters who can afford few other foods. The clinical picture is almost always one of a multiple nutritional disorder, although lack of thiamine (aneurine) produces the predominant clinical changes. The disease rarely occurs among people who are markedly underfed. Much more important is the gross disproportion between the amount of carbohydrate in the diet and the quantity of thiamine available to ensure its complete metabolism. Hence the disease may be precipitated by an increase in the ration of rice or other foods rich in carbohydrate. Thiamine is required by the human body because it is an essential component of the enzyme systems concerned with the utilization of carbohydrate. [illegible] eliminate with sufficient speed the products of carbohydrate catabolism. These products are vasodilators and may cause extreme dilatation of the peripheral vascular bed; in consequence œdema develops though the plasma proteins may be unaltered and the heart initially unembarrassed. The œdema affects the dependent extremities, but shifts less rapidly than does famine œdema (less wasting and laxity of superficial tissues); because of the vasodilatation the swollen legs are hot to the touch. The quick disappearance of blood into the

dilated capillaries gives rise to " pistol-shot " sounds heard by auscultation over the femoral arteries and to an unusually rapid circulation time. The rate at which the blood circulates places a burden on the heart which is already working at a disadvantage, since the myocardium cannot catabolize carbohydrate normally. Cardiac dilatation and failure ultimately result and may cause sudden death; hence it must be recognized that the patient with signs of beriberi heart is perilously ill. Immediate bed rest is essential and thiamine should be given at once to correct the causative biochemical lesion. Thiamine hydrochloride 10 mg. daily, given intramuscularly, has been shown to bring dramatic relief in the majority of cases. Vasodilatation is relieved and there is usually a rapid diuresis Larger doses of thiamine should be avoided, untoward reactions to excessive parenteral doses have been reported. When thiamine fails to produce the

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Nervous System.

Pellagra.—This is a disease of maize-eaters Maize (Indian corn) is a good food if included in a well-balanced diet. However, when it is relied upon as the principal source of calories, it produces nutritional failure because it lacks certain essential amino acids, notably tryptophan, and it contains a potentially poisonous substance, probably an antagonist (antivitamin) to nicotinic acid. Typically, the patient with pellagra suffers from multiple dietary deficiencies.

The classic features of pellagra are · non-infective inflammation of the entire gastro-intestinal tract producing a red, swollen " raw beef " tongue and diarrhœa, erythema of exposed parts of the skin, often with secondary infection; and mental changes—depression and anxiety, but practically never dementia. These abnormalities often yield dramatically to rest in bed and the administration of nicotinic acid—giving the laboratory worker the erroneous impression that the clinician has cured the patient by this treatment alone, whereas the experienced clinician knows that the correction of other dietary deficiencies contribute to the cure.

The human body uses nicotinic acid as an essential part of one of the enzyme systems concerned with tissue oxidation In normal circumstances it can make at least a substantial part of its requirements for this nutrient from the amino acid, tryptophan, and it is probably assisted in this task by the metabolic activity of the bacteria in the intestines. An old and tried clinical observation is that milk

often dramatic. It should be given by mouth, in doses of

throughout the day, for a few days, after which the patient is more co-operative, his erythema relieved and his diarrhœa turned to constipation. Yet he is still a sick man: he will be found frequently to suffer from anæmia due to lack of iron and hypoproteinæmia due to prolonged protein deficiency. Once again, the patient needs more treatment than the simple prescription of a single vitamin. In this treatment a good diet, including plenty of milk supplemented by products of yeast, liver or the germ of cereals, is more important than the continued administration of nicotinic acid

Angular Stomatitis and Cheilosis.—Soggy, grey fissures at the corners of the mouth (angular stomatitis) and red, denuded epithelium at the line of closure of the lips (cheilosis) are frequently seen in pellagrins, as in other patients with debilitating diseases In pellagrins they have been reported to respond well to riboflavin (e.g. 10 mg a day by mouth), but also equally well to pyridoxine. The commonest cause of angular stomatitis in Britain is ill-fitting dentures.

Other clinical disorders sometimes associated with beriberi and pellagra and attributed to dietary deficiencies of various components of the vitamin B complex are discussed later in this chapter

Kwashiorkor.—This is a disease of young children, first fully studied on the Gold Coast by Williams in 1933 and now known to be world-wide in its distribution. It occurs wherever children are weaned on a diet containing little else than roots such as cassava, or cereals such as maize, poor in essential amino acids It has all the features of famine œdema with the additional characteristic of a large, palpable liver. Without adequate dietetic treatment there is frequently death, and cirrhosis of the liver among the survivors There is no evidence as yet that the disease is due to lack of any one specific nutrient; but it has been established beyond doubt that skimmed milk in small amounts is curative in early cases. Concentrated vitamin preparations have been reported to be positively harmful in the early stages of treatment, but may be given during convalescence if thought necessary

Rickets.—This is the pale counterpart of kwashiorkor in temperate climates, in terms of total infantile deaths it is a far less important disease It arises in the same circumstances when infants are weaned on predominantly cereal diets and receive insufficient milk to provide calcium for the formation of the skeleton. Lack of available calcium during the growing period of life results in the bony deformities of rickets, and these, if not corrected early, will be permanent Lack of vitamin D is often an important cause of rickets because this vitamin assists the absorption of calcium from the bowel. Vitamin D can be synthesized [illegible]

is the best supplement. Two teaspoonfuls (about 8 ml) daily of a B.P. preparation will provide at least 600 International Units of vitamin D, which is a satisfactory prophylactic dose for a child of six months. In addition, cod-liver oil provides useful amounts of digestible fat and vitamin A. In some countries it is necessary to remember that cod-liver oil may be so diluted with vegetable oils

that its antirachitic potency is negligible. For severe cases the synthetic vitamin calciferol is preferable ; a suitable daily dose is [illegible]
of vitamin D (B.P.), whic
massive dose, e g. 100,000
and curative effects in times of emergency such as famine when there is little chance that the infant will receive adequate medical care in future. It should be remembered, however, that *excessive doses of calciferol produce metastatic* calcification and other poisonous effects.

Osteomalacia or adult rickets, due solely to dietary causes, is practically confined to women who live in purdah in the poorest quarters of the industrial cities of the East and have numerous pregnancies. The [illegible]
clearly of the greatest importance.
orthopædic management is needed
vitamin D.

Conditioned Rickets and Osteomalacia.—Various diseases predispose to the development of clinical rickets ; the commonest is cœliac disease and in adults, sprue Here the administration of synthetic calciferol is especially valuable, as the patient will not readily tolerate the fats contained in natural sources of vitamin D. These diseases are discussed above. There are several rare pathological conditions in which chronic impairment of renal function results in demineralized bones. In renal acidosis the tubules have lost the power of substituting ammonia for the base that is normally largely reabsorbed from the glomerular filtrate; consequently excessive amounts of base, including calcium, are lost in the urine. At the same time, part of the acids which would normally be excreted in the urine are reabsorbed by the tubules, since no ammonia is available to neutralize them The result is that the urine is deficient in acid radicals, which are retained in the body, producing an acidosis ; whilst *the excessive* loss of calcium in the urine withdraws calcium *from* the bones, producing conditioned osteomalacia. Acidosis is also present in " renal rickets ", [illegible]
standing [illegible]
acid meta
secondary hyperparathyroidism with consequent withdrawal of calcium from the bones and the development of conditioned osteitis fibrosa (p. 371).

[illegible]
unable to reabsorb, among other things, amino acids, phosphorus and glucose. Because of the constant glycosuria there is often chronic ketosis and ketonuria. The excessive excretion of such acid radicles may lead to the withdrawal of calcium from the bones to neutralize them The result is conditioned osteomalacia, though without acidosis. Another medical curiosity is osteomalacia appearing in well-fed adults because they are " vitamin D resistant ". Nevertheless, they respond to massive doses of calciferol (e g 100,000 I U. daily, [illegible] by mouth)
ubsisting on predominantly

Diseases due to an Insufficient Consumption of Fruit and Vegetables.
Scurvy—Scurvy has been recognized as a clinical entity since mediæval times, arising whenever war or natural disaster cut off the supply of fresh food. It came into prominence when sailing-ships began to open up the great oceans of

scurvy could be relieved by the juice of citrus fruits But he did not make the modern mistake of concluding that scurvy was therefore due solely to lack of

The part played by such factors in depleting the suprarenal cortex of ascorbic acid has only lately been recognized It is necessary to emphasize, however, that stress, even of the most severe kind, will not cause scurvy if the previous diet has provided adequate amounts of ascorbic acid.

The normal human body when fully saturated with the vitamin contains about 5 g ; treatment should therefore aim at achieving saturation, by giving 1 g. daily in four divided doses for about a week. When large single doses are given,

value are orange juice, rose-hip syrup, extract of pine needles and sprouting pulses Ascorbic acid—as it occurs naturally or as the synthetic preparation—brings to an end the characteristic bleeding into the tissues Once the hæmorrhagic manifestations are under control, it remains to the physician to remedy so far as he can the environmental factors that conditioned the disorder and to attend to the other dietary deficiencies which are almost invariably present.

Xerophthalmia and Allied Disorders—Coloured fruits and vegetables contain carotene, the precursor of vitamin A The body can use carotene as an alternative to the pre-formed vitamin which is found only in animal fats. Disorders due to deficiency of this vitamin occur most often when the diet lacks both dairy produce and fruit and vegetables Characteristically they arise in hot dry climates. These disorders are described below under Nutritional Disorders of the Eye and Skin.

Nutritional Disorders of the Skin.—Various changes may be seen in examining the skin of patients who are undernourished or malnourished. The thin, dry, inelastic, pigmented skin of the starving has already been mentioned on p 334. The loose skin-folds, lacking subcutaneous fat, of the underfed patient are familiar. Simple atrophy, in which the skin appears thin and tightly stretched, especially on the legs, is sometimes seen in malnourished people. Dryness of the skin (xeroderma) may be associated with an appearance as though a layer of lacquer had been painted on, and then had dried, leaving a "crazy paving" design ("crackled skin"). This is often accompanied by a fine, brawny desquamation. There may be thickening and roughening of the skin over the elbows, knees, insteps and other bony prominences ("elephant skin"). The follicles may be blocked with horny plugs of keratin (follicular keratosis);

in the diet. Follicular keratosis certainly occurs in vitamin A deficiency and, when due to this cause, is curable with therapeutic doses of the vitamin (see

hæmorrhages, characteristic of this disease, commonly first appear. Yet many normal people have folliculosis. Nicol, in Nigeria, has shown that crackled skin and elephant skin occur less commonly in Africans using red palm oil (rich in vitamin A) than in others.

should draw attention to the patient's diet. In this way they are useful signs; they emphasize again that the aim of medicine is to treat the patient and not merely a particular tissue.

Chilblains (p. 622) are unusually common among people who are severely undernourished; *they may be preceded by cyanosis of the fingers and toes, even* in warm weather. But this does not prove that dietary factors are always involved in their production They occur among people who by every other criterion seem adequately nourished. The very variety of nutrients offered for their relief —calcium, nicotinamide, vitamins D, E and K—indicate that none is effective.

Oro-genital Syndrome.—Stannus first described this condition in 1912 as a nutritional disease of Africans. It has since been reported in many parts of the world and is apt to appear wherever diets are seriously deficient in the vitamin B complex. There is usually angular stomatitis, cheilosis (p. 341) and glossitis There may be a scaly, greasy dermatitis around the sides of the nose, on the lips, a

ay appear only below the waist. Though a few physicians have reported benefit from the prescription of pure synthetic riboflavin alone, all are agreed that yeast extract (e g. Marmite) is

small abrasion.

light plaster to avoid frequent changes of dressings which inevitably introduce additional bacterial flora The lesion is unlikely to heal satisfactorily unless the patient is given a good diet; indeed, it may progress to kill the malnourished

patient, invading deeply into the tissues, destroying bone and causing fatal septicæmia.

Impetigo, Furunculosis and other skin infections are particularly common among the malnourished. In such patients local treatment will be unavailing unless attention is also paid to their diet. Vitamin A in therapeutic doses (see below under xerophthalmia) is often especially useful in treating skin infections among people living on poor diets in hot, dry climates.

The dermatitis of pellagra is mentioned on p. 340.

Nutritional Disorders of the Eye.—*Nutritional Amblyopia (Retrobulbar Neuropathy).*—This distinct clinical entity was first fully studied by Fitzgerald Moore among West Africans. It became extremely troublesome among prisoners in Japanese hands during the late war. The first symptom is blurred vision, often with photophobia and aching at the back of the eyes. On examination, central or paracentral scotomata are found. Irreversible optic atrophy may result if the disease remains untreated for a year or more.

There can be no question that the primary cause of this disease is nutritional. Lack of one or more components of the vitamin B complex is almost certainly responsible. The disease has been reported in association with beriberi and pellagra, though it often occurs quite independently. Vitamin A, synthetic thiamine and nicotinic acid have all been tried and found to be useless in its treatment. On the other hand, good results have been repeatedly obtained with yeast extract (Marmite). In Changi prison, Singapore, an extract of green leaves containing riboflavin was found beneficial.

The possibility of a toxic factor (e.g. tobacco) contributing to the disorder should be kept in mind, in individual cases.

Xerophthalmia.—This disease, made famous by physiologists, is found among people whose diet is grossly deficient in dairy produce, fish, fruit and vegetables. It rarely affects the cornea. The ducts of the tear glands become blocked with keratin and consequently the anterior surface of the eye is dry. The scleral conjunctiva takes on a "ground glass" appearance and becomes thickened and easily thrown into folds by the gentle pressure of a finger. There may be small, clear-white flecks of altered epithelium fixed to the scleræ (Bitôt's spots). In advanced cases only the cornea is softened (keratomalacia), perhaps due to lack of riboflavin (see below).

Xerophthalmia responds quickly and well to vitamin A. About 250,000 International Units given by mouth in divided doses over a period of a week are curative. The cheapest and most convenient source of the vitamin is usually halibut-liver oil, though in some countries shark-liver oil or red palm oil may be easier to obtain.

Hemeralopia ("night blindness").—This symptom has several causes unconnected with nutrition (e.g. retinitis pigmentosa). But it may arise under the same conditions that produce xerophthalmia and often precedes it. Vitamin A is an essential component of the retinal pigment, visual purple, on which vision in dim light depends. Again, 250,000 I.U. of vitamin A by mouth is generally curative—if the cause is nutritional.

Vascular Cornea.—The cornea, which is normally avascular, sometimes becomes invaded by minute capillary vessels, visible with a slit-lamp. This change, generally attended by photophobia and lachrymation, sometimes occurs in association with the oro-genital syndrome (see p. 344). At one time it was regarded as a specific sign of riboflavin deficiency. Though it has been reported

to respond to riboflavin (e.g. 5 mg three times daily by mouth) in patients whose diet has been deficient in this vitamin, in other cases this treatment has proved disappointing

Nutritional Keratitis (corneal degeneration, keratomalacia).—A lesion of the cornea, distinct from xerophthalmia, developed among the inmates of Japanese prison camps and also occurs in Bantus. Minute greyish punctate patches, usually staining with fluorescein, appear in the cornea and most often in the lower portion, unlike trachoma. These may go on to coalesce, interfering with [illegible]

associated component of the vitamin B complex. Yeast extract and rice polishings have been found to be beneficial

Most sufferers from trachoma are malnourished, but as yet there is no evidence that deficiency of any specific nutrient predisposes to this infection.

Nutritional Disorders of the Nervous System.—*Nutritional Polyneuropathy.*—This disease is classically associated with the prolonged consumption of diets composed chiefly of rice and a few vegetables poor in protein and vitamins of the B complex. Weakness and paræsthesia progress frequently to foot drop, loss of tendon reflexes and symmetrical peripheral anæsthesia; nerve deafness is a common accompaniment. The disorder may arise as a conditioned deficiency due to chronic alcoholism, vomiting of pregnancy or chronic pyloric obstruction It sometimes occurs in association with "wet" cardiovascular beriberi, for which reason it has been unfortunately called "dry beriberi", a name that is better avoided because it suggests that the two diseases are the same and have a common ætiology, whereas they are quite distinct. Cardiovascular beriberi occurs typically in patients who are well-fed having lived on a diet rich in rice or other sources of carbohydrate, though poor in the vitamin B complex By contrast, cases of nutritional polyneuropathy are characteristically severely underfed, weak and wasted, and they rarely present evidence of the disordered carbohydrate metabolism characteristic of wet beriberi

Thiamine (vitamin B_1) is of little use in treating nutritional polyneuropathy. Though it once enjoyed a great vogue as the "anti-neuritic vitamin", this was based all along on a misunderstanding. The laboratory workers in their search for the dietary factor that would prevent peripheral neuropathy in animals finally isolated thiamine as the factor that would prevent not a peripheral but a central lesion of the nervous system—an encephalopathy. Animals deficient only in thiamine have no histological changes in their peripheral nerves; on the other hand, typical polyneuropathy, has been produced experimentally by diets containing abundant thiamine but deficient in other components of the vitamin B complex

Wernicke's Encephalopathy and Allied Conditions.—The human counterpart [illegible]

[illegible] ophthalmoplegia and "cog-wheel" rigidity of the extremities At autopsy, dilatation of the capillary blood vessels in the nuclei of the brain-stem gives evidence of an acute failure of carbohydrate metabolism. Thiamine hydrochloride parenterally (e g. 10 mg. intravenously, three times daily) often relieves

the gross manifestations of this disease, although the patient does not recover until the whole vitamin B complex is supplied in the form of yeast extract, rice polishings or wheat germ.

The cause of nutritional polyneuropathy remains in doubt; several factors are probably involved and may include multiple deficiencies of the vitamin B complex, subnutrition and insufficiency of tissue enzymes due to inadequate protein intake. It may be that lack of such enzymes may render the nerves susceptible to potential poisons in the diet, including alcohol itself. The part played by dietary deficiencies in the causation of Korsakoff's psychosis and delirium tremens is indefinite, attention to the diet is certainly desirable in both conditions, and plenty of milk should be given, but no single nutrient is especially useful.

Treatment of Nutritional Polyneuropathy.—This demands, first, attention to the patient's diet both in quality and quantity. The nerve lesions will not improve until the patient regains his strength Every effort should be made to restore him to the body-weight appropriate for his height; but obesity must not be allowed to develop Plenty of protein (milk, eggs, meat, fish) is needed, supplemented by natural sources of the vitamin B complex; yeast extract (Marmite), liver extract, rice polishings or wheat germ Muscular activity should be encouraged and deformities must be prevented Skilled physiotherapy may therefore be needed

"Burning Foot" Syndrome.—Intensely painful extremities, sometimes associated with exaggerated tendon reflexes but often without physical signs, was a distressing disorder of prisoners in Japanese hands and also occurs endemically among the Tamils of Southern India. Its most probable cause is a disturbance of the sympathetic innervation to the peripheral blood vessels. Relief has been reported following the administration of pantothenic acid (20 mg. calcium pantothenate intramuscularly daily), but again, the essence of treatment is attention to the diet and improvement in its content of the entire vitamin B complex.

Disorders of the Spinal Cord.—Signs of involvement of tracts in the spinal [illegible]

lathyrism—a disease that occurs in epidemics during famines. Lathyrism is due to excessive consumption of the lathyrus pea: this contains a toxic substance which selectively damages the pyramidal tracts of underfed people. The possibility of the existence of a poisonous factor in the diet should always be kept in mind in cases of nutritional spastic paraplegia. Sometimes the principal lesion is in the posterior columns of the cord producing a spinal ataxia, resembling subacute combined degeneration of the cord, but not necessarily associated with anæmia or achlorhydria In such cases it would seem reasonable to administer cyanocobalamin (pp. 414, 419) as a supplement to a good general diet.

DISEASES DUE TO POISONOUS SUBSTANCES IN FOOD

Many wholesome foods contain potentially poisonous substances. For instance rhubarb and spinach contain oxalic acid; the potato has a poisonous alkaloid; cassava, from which tapioca is prepared, contains cyanide. But the traditional methods of preparing such foods usually result in the elimination of the poisonous factor. Moreover the well-nourished body has no difficulty in

finding metabolic means of detoxicating small amounts of the poison. A medical problem arises only when the metabolic defences of the body are impaired by malnutrition and the quantity of poison ingested is greater than usual. It is a fair generalization to say that, apart from bacterial contamination, food poisoning rarely occurs except at times of food shortage. Thus ergotism swept through mediæval Europe when the rye crop was bad and infected with ergot. The poisonous effects of the lathyrus pea become manifest only in times of famine. *In nutritional amblyopia and polyneuropathy a toxic factor may yet be found to* play a part. Even in pellagra, it is now fairly certain that maize contains an

The Sophistication of Food.—In modern food processing there is an increasing tendency to take things out of food and sometimes to give back others in an attempt to replace what has been lost, as in the "fortification" of bread with synthetic vitamins. Chemicals are often added to food as preserving agents,

The doctor cannot hope to change the nation's food habits or the current practice of the food industry overnight. However, he should remember that patients on short commons are more liable than others to food poisoning; and he should warn them to beware of new and untried sophisticated foods.

NUTRITIONAL DISORDERS IN WESTERN MEDICAL PRACTICE

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rhœa, *the polyneuropathy that follows chronic pyloric obstruction and the manifold* nutritional disorders that may attend chronic alcoholism. People who habitually rely upon alcohol to provide the chief portion of their daily calories, lack other nutrients; they may develop scurvy, pellagra, beriberi or polyneuropathy, *depending on* their habits and, perhaps, constitution.

In all such cases of conditioned nutritional disorders, treatment should first be directed to removing the underlying cause; thereafter it should proceed along the lines indicated above *for the relief of the same disorders arising primarily* from faulty diet

"Sub-Clinical" Nutritional Disorders.—Ever since the first introduction of synthetic vitamins, a great deal of propaganda has been pressed on the profession to encourage the belief that any patient who is tired or out of sorts may be suffering from a mild vitamin deficiency. This idea gains ready acceptance among patients who find, late in life, that they must modify their established eating habits because of the rising cost of food. *In fact, serious vitamin deficiency* disorders are extremely rare in Britain and, by inference, minor deficiencies must

be uncommon; whoever heard of an endemic disease that manifests itself solely as *formes frustes*? Analysis of the diets eaten by patients in Britain usually shows that they provide a fair supply of the essential vitamins. The exception is that, in Scotland particularly, people sometimes do not obtain

tonics is poor practice because it is lazy; it saves the physician the trouble of dealing radically with the patient's problem, which may only indirectly involve his diet. In any case, pills and capsules containing various mixtures of pure synthetic vitamins are

preparations is deplor

ever has to pay for it;

that he has done all that is necessary for the proper nutrition of his patient. "Multi-vitamin" preparations vary widely in composition; they may lack the particular vitamin (perhaps not available in synthetic form) which might conceivably help the patient and they may create a state of vitamin imbalance by providing an excess of others. Finally, it has yet to be learned what harmful effects may attend the prolonged consumption of these potent chemicals in excess of physiological needs, the bacterial flora of the intestines ordinarily make significant amounts of several vitamins, apparently useful to their host. But if these bacteria are continually bathed in an artificial medium of synthetic vitamins, it is within the pattern of biological behaviour that they may mutate, with incalculable metabolic consequences

The proper treatment of subnutrition and malnutrition continues to rest on attention to the patient's diet When the diet has been deficient in some important respect, the first line of treatment is to supply the food that is lacking Thereafter, special shortages may be replaced by the following:—proteins, by dried milk or milk products, fat-soluble vitamins, by fish-liver oils, ascorbic acid, by orange juice, black-currant and rose-hip syrup or extract of pine needles; the vitamin B complex, by yeast or yeast extract (e g. Marmite), liver, rice polishings or wheat germ. The synthetic vitamins are useful in the immediate relief of the classic nutritional diseases—pellagra, beriberi, rickets and scurvy—but they have little other value.

Use of Vitamins as Drugs.—There has been a tendency in the past to use

abortion, coronary artery disease, etc., yet there is no proof that it is a necessary component of human diet At present there is only one clear indication for the

vitamins, is not excreted in the urine if taken in excessive amounts and so can accumulate in high concentrations in the body and occasionally produce toxic effects The prescribing of large doses of water-soluble vitamins has at least this safety-valve, that the body eliminates them rapidly; but imagination boggles

at the thought of the pounds-worth of unwanted synthetic water-soluble vitamins that are still daily lost in human urine!

In previous editions of this textbook, the chapter which this supersedes was written by the late Professor Noah Morris In it he said, "When a mild deficiency state exists it can easily be eliminated in the majority of cases by the provision of an adequate mixed diet without having to resort to special vitamin preparations. Although a platitude, it seems necessary to keep on reiterating that proximate principles and calories are as essential as vitamins." This is one of the platitudes which happens to be true.

A. P. Meiklejohn.

DISEASES OF THE DUCTLESS GLANDS

THE THYROID GLAND

SIMPLE GOITRE

SIMPLE GOITRE is probably due to a temporary deficiency of circulating thyroxine. This deficiency stimulates an increased secretion of thyrotrophin from the anterior pituitary which causes enlargement of the [illegible]

[illegible] from many foods and to a lesser degree from water Iodine deficiency may be absolute in cases where the iodine intake is subnormal Under such circumstances endemic goitre is common, and its highest incidence is observed in the Alps, the Pyrenees, and Himalayas, in certain districts of New Zealand and round the Great Lakes of the United States. Iodine deficiency may, however, be relative and may ensue whenever gastro-intestinal absorption is inadequate. The most common cause of this is a diet high in calcium—particularly hard drinking-water—which may prevent the proper absorption of iodine. (2) The ingestion of antithyroid substances may block the synthesis of thyroxine. A large number of such substances are known to exist among foodstuffs and drugs. Cabbage, turnip, cobalt, thiourea derivatives, sulphonamides, and para-aminosalicylic acid (PAS) may be mentioned as examples. (3) An increased demand for thyroid hormone may make a previously sufficient intake inadequate. Such increased demands may occur during the course of prolonged fevers, at puberty and during pregnancy and lactation. (4) There may be an inherent biochemical defect in the thyroid which prevents it from synthesizing an adequate amount of thyroxine in the normal manner It seems probable that when simple goitre occurs in non-endemic areas the items mentioned under 3 and 4 constitute the most important ætiological factors.

Prophylaxis.—The quantity of iodine required per day by a human being is extremely small. The minimum daily requirement is about 200 microgrammes for an average adult, and this is very amply met if adequately iodized salt is consumed The Medical Research Council recommend the addition of either 1 part of potassium iodide to 100,000 parts of all common table salt sold, or 1 part to 40,000 parts of all packeted table salt. It is disappointing that an agreement between the Ministry of Health and the salt manufacturers for the addition of iodide to salt, promised for 1952, has not at the time of writing been implemented. The pregnant woman should receive an additional supply and traces of potassium iodide are added to the vitamin A and D tablets issued for expectant mothers The prevention of endemic goitre and its sequelæ will depend not only on the preparation and consumption of adequately iodized salt [illegible]

world.

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demand for thyroid hormone may make a previously sufficient intake inadequate. Such increased demands may occur during the course of prolonged fevers, at puberty and during pregnancy and lactation (4) There may be an inherent biochemical defect in the thyroid which prevents it from synthesizing an adequate amount of thyroxine in the normal manner. It seems probable that when simple goitre occurs in non-endemic areas the items mentioned under 3 and 4 constitute the most important ætiological factors.

Prophylaxis.—The quantity of iodine required per day by a human being is extremely small. The minimum daily requirement is about 200 microgrammes for an average adult, and this is very amply met if adequately iodized salt is consumed. The Medical Research Council recommend the addition of either 1 part of potassium iodide to 100,000 parts of all common table salt sold, or 1 part to 40,000 parts of all packeted table salt It is disappointing that an

expectant mothers. The prevention of endemic goitre and its sequelæ will depend not only on the preparation and consumption of adequately iodized salt but also on the persistent education by doctors of all peoples as to the necessity for its use. Universal legislation to give effect to this simple and harmless measure would result in the effective control of endemic goitre throughout the world.

at the thought of the pounds-worth of unwanted synthetic water-soluble vitamins that are still daily lost in human urine !

In previous editions of this textbook, the chapter which this supersedes was written by the late Professor Noah Morris. In it he said, " When a mild deficiency state exists it can easily be eliminated in the majority of cases by the provision of an adequate mixed diet without having to resort to special vitamin preparations. Although a platitude, it seems necessary to keep on reiterating that proximate principles and calories are as essential as vitamins." This is one of the platitudes which happens to be true.

A. P. MEIKLEJOHN.

DISEASES OF THE DUCTLESS GLANDS

THE THYROID GLAND

SIMPLE GOITRE

SIMPLE GOITRE is probably due to a temporary deficiency of circulating thyroxine. This deficiency stimulates an increased secretion of thyrotrophin from the anterior pituitary which causes enlargement of the thyroid, and the consequent improvement in the amount of circulating thyroxine maintains a euthyroid state. The initial deficiency of thyroid hormone may be due to a number of causes. (1) Endemic goitre is usually due to a deficiency of *iodine, which is essential for the formation of thyroxine. Iodine is obtained* from many foods and to a lesser degree from water Iodine deficiency may be absolute in cases where the iodine intake is subnormal Under such circumstances endemic goitre is common, and its highest incidence is observed in the Alps, the Pyrenees, and Himalayas, in certain districts of New Zealand and round the Great Lakes of the United States. Iodine deficiency may, however, be [illegible] quate. [illegible] hard [illegible]) The ingestion of antithyroid substances may block the synthesis of thyroxine A large number of such substances are known to exist among foodstuffs and drugs. Cabbage, turnip, cobalt, thiourea derivatives, sulphonamides, and para-aminosalicylic acid (PAS) may be mentioned as examples. (3) An increased demand for thyroid hormone may make a previously sufficient intake inadequate. Such increased demands may occur during the course of prolonged fevers, at puberty and during pregnancy and lactation. (4) There may be an inherent biochemical defect in the thyroid which prevents it from synthesizing an adequate amount of thyroxine in the normal manner. It seems probable that when simple goitre occurs in non-endemic areas the items mentioned under 3 and 4 con- [illegible]

[illegible]

grammes for an average adult, and this is very amply met if adequately iodized salt is consumed. The Medical Research Council recommend the addition of either 1 part of potassium iodide to 100,000 parts of all common table salt sold, or 1 part to 40,000 parts of all packeted table salt. It is disappointing that an agreement between the Ministry of Health and the salt manufacturers for the addition of iodide to salt, promised for 1952, has not at the time of writing been implemented. The pregnant woman should receive an additional supply and traces of potassium iodide are added to the vitamin A and D tablets issued for expectant mothers. The prevention of endemic goitre and its sequelæ will depend not only on the preparation and consumption of adequately iodized salt but also on the persistent education by doctors of all peoples as to the necessity for its use. Universal legislation to give effect to this simple and harmless measure would result in the effective control of endemic goitre throughout the world.

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Treatment consists in administering thyroid extract or thyroxine in daily doses of 0·2 g. (3 gr.) and 0·3 mg respectively.

Chronic Fibrous Thyroiditis.—This rare condition produces signs and symptoms which closely resemble carcinoma of the thyroid, since the gland is stony hard and gives rise to pressure symptoms. When these latter are severe, subtotal thyroidectomy should be undertaken.

CRETINISM

There are two types of cretinism—endemic and sporadic. The former results from iodine deficiency in the mother, tends to occur in goitrous families and the cretin itself is frequently goitrous The latter occurs as the result of a defect in thyroid development, the parents are euthyroid and the cretin usually has no thyroid The successful treatment of either type depends upon early diagnosis and the adequate administration of thyroid throughout the lifetime of the patient. As cretinism in this country is sporadic and rare, it is much more likely to escape detection in its early stages than in countries where it is endemic and relatively common. The untreated cretin, over two or three years of age, presents a classical clinical picture, but during the first year of life, when adequate treatment offers the most favourable prognosis, the physical signs are much more equivocal

The brain of a normal infant develops with great rapidity during the first

chance of entirely successful mental development As diagnosis is rarely made until much later, however, only a small percentage of cretins grow up mentally normal. The majority remain more or less retarded with an intelligence quotient of below 70 per cent., the extent of the mental defect depending largely on the length of time which elapses before the start of treatment Although early treatment is essential if full mental development is to result, a cretin may remain untreated until the age of four and yet show skeletal growth to almost normal proportions under proper treatment. The administration of thyroid to untreated cretins over the age of twelve is often worse than useless Usually it only

patient. The correct dose is that which will allow of normal growth and development without producing signs of hyperthyroidism The amount required varies with the age and weight of the child from about 6 mg ($\frac{1}{10}$ gr.) daily in early infancy to doses of 0·06 to 0·2 g (1 to 3 gr.) daily in late childhood. All references are to the B.P. preparation. This is a dried extract, standardized to contain 0·1 per cent. of iodine in combination as thyroxine. Non-official preparations vary considerably in potency, and unless this is stated by the manufacturers in terms of the B.P. standard, such preparations should not be used.

natural preparation in the course of time just as digoxin is being used more and more in preference to digitalis. 0·1 mg of thyroxine is equivalent to 60 mg. (1 gr.) of thyroid A very small dose of thyroid or thyroxine is sufficient to

Curative.—Whatever be the cause of a simple goitre, a relative deficiency of thyroxine is involved with consequent excess secretion of thyrotrophin. Treatment must, therefore, involve the administration of thyroid extract or synthetic thyroxine. It is seldom necessary to give more than 0 2 g. (3 gr.) of the former or 0 3 mg of the latter daily, though cases do occur of unusual resistance to these drugs and larger doses may then prove necessary. The reason for this therapy is not so much to replace thyroxine, which is already being adequately produced if the patient is euthyroid, but to inhibit the production from the pituitary of thyrotrophin, and so to cause a reduction in the size of the thyroid gland. In addition, 60 mg. (1 gr.) of potassium iodide should be given daily to ensure that any iodine deficiency which may be present is corrected. Proof is entirely lacking that iodine-induced hyperthyroidism (Iodine-Basedow)—a condition greatly feared upon the Continent—ever occurs as the result of this relatively large dose, and there is a great deal of cogent evidence to the contrary.

The slight enlargements of the thyroid which so commonly occur at puberty and during pregnancy and lactation respond regularly to treatment with thyroid and iodine, and similar treatment should be given to patients with larger diffuse or even nodular simple goitres. In general, the larger the goitre the longer will be the necessary period of treatment which may have to be continued from six to twelve months. Even then it is usually unsuccessful if the goitre has been present for a considerable time.

When the goitre persists in spite of adequate treatment, and especially if compressive symptoms develop, surgery is required. There is a common belief that such simple diffuse or nodular goitres require no treatment except for cosmetic purposes. This belief is probably fallacious A large proportion of simple goitres become adenomatous. Some 25 per cent. of these eventually become toxic, while a very small number undergo malignant change. Thus the prophylaxis of simple goitre and its efficient medical treatment, or its surgical removal when persistent, constitute the prophylaxis of thyrotoxic adenomata and of thyroid carcinoma.

THYROIDITIS

Thyroiditis is a rare disease. The forms encountered are: (1) giant-cell thyroiditis; (2) chronic lymphoid thyroiditis (Hashimoto's struma); (3) fibrous thyroiditis (Riedel's struma).

Giant-Cell Thyroiditis.—In this condition a greater or less degree of non-suppurative necrosis of the thyroid occurs, resulting in pain, tenderness, fever and swelling. Thyrotoxicosis is a very rare concomitant feature.

The condition usually subsides spontaneously in the course of time without treatment, but this process may be accelerated by the daily administration of 100 mg. of prednisone for two or three weeks, followed by 0 2 g. (3 gr) of thyroid extract as 0 3 mg. thyroxine daily for two or three months. Antibiotic treatment is usually unnecessary

Chronic Lymphoid Thyroiditis.—This disorder should be suspected when a middle-aged woman is found to have a nodular goitre in association with symptoms of hypothyroidism and dysphagia The diagnosis is usually made [illegible]

Treatment consists in administering thyroid extract or thyroxine in daily doses of 0·2 g. (3 gr.) and 0·3 mg. respectively.

Chronic Fibrous Thyroiditis.—This rare condition produces signs and symptoms which closely resemble carcinoma of the thyroid, since the gland is stony hard and gives rise to pressure symptoms. When these latter are severe, subtotal thyroidectomy should be undertaken.

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The quantity of thyroid required is usually gauged by the response of the patient. The correct dose is that which will allow of normal growth and development without producing signs of hyperthyroidism. The amount required varies with the age and weight of the child from about 6 mg. ($\frac{1}{10}$ gr.) daily in early infancy to doses of 0·06 to 0·2 g. (1 to 3 gr.) daily in late childhood. All references are to the B.P. preparation. This is a dried extract, standardized to contain 0·1 per cent. of iodine in combination as thyroxine. Non-official preparations vary considerably in potency, and unless this is stated by the manu-

natural preparation in the course of time just as digoxin is being used more and more in preference to digitalis. 0·1 mg. of thyroxine is equivalent to 60 mg. (1 gr.) of thyroid. A very small dose of thyroid or thyroxine is sufficient to

banish the grosser stigmata of cretinism and to effect a remarkable improvement, but the practitioner should not be content with the mere disappearance of symptoms, since a dose sufficient to dispel symptoms may be inadequate to ensure satisfactory growth and osseous development. The rule which should govern the administration of thyroid in cretinism is quite different from that in adult myxœdema, in which the smallest dose which will keep the patient free from hypothyroid symptoms should be given. In cretinism the largest dose consistent with freedom from thyrotoxic symptoms should be administered.

up until mild toxic symptoms appear, and then, after a few days' freedom from treatment, a maintenance dose just below the toxic level should be given. The initial dose of thyroid should nevertheless be small, since subthyroid cretins are much more sensitive to thyroid medication than those whose metabolism has been raised to normality by appropriate treatment. A large initial dose in an untreated case may result in alarming toxic symptoms. It should be remembered also that it takes fully a month for a daily dose of thyroid to exert its maximum effect. The dose should not therefore be increased until this period has elapsed. The patient's growth and osseous development should be checked by careful measurements, and by an X-ray examination every six months. Inadequate development is usually due to inadequate dosage. It cannot be too strongly emphasized to the parents that it is necessary to continue the daily administration of thyroid throughout the life of the patient. The dramatic improvement, which results from properly controlled treatment, is apt to encourage the belief that permanent "cure" has resulted, and that treatment can be discontinued.

MYXŒDEMA

Juvenile Myxœdema.—Sometimes a clear distinction is not made between cretinism and juvenile myxœdema: in the former the thyroid is deficient from birth; in the latter it becomes deficient after a number of years in which mental and physical development have progressed normally. The prognosis is much better than in cretinism, as permanent damage to the central nervous system is not so apt to result from a deficiency of thyroid secretion in later childhood or adolescence as it is from a similar deficiency during the critical months of infancy.

As in cretinism, dosage with thyroid should be the maximum consistent with the avoidance of toxic symptoms. From 0.1 to 0.2 g. (1½ to 3 gr.) will usually

ated. Severe

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by frequent measurements and radiological examinations to ensure that osseous development is proceeding normally.

Adult Myxœdema.—Adult myxœdema may be due to a primary idiopathic atrophy of the thyroid, to therapeutic thyroidectomy, to excessive dosage with

to hypopituitarism (see p. 377) in which failure of secretion of thyrotrophin occurs.

There are few conditions in which the response to treatment is so gratifying as in primary myxœdema in the adult. The simple oral administration of thyroid or thyroxine will relieve symptoms entirely: within a week of starting treatment the patient's appearance improves; the speech is clearer and the mental functions brighter, cold is felt less, the appetite improves and constipation is relieved, some loss of weight occurs, principally owing to free diuresis to be followed often by a gain in weight due to improved nutrition; and psychotic manifestations, which are not at all uncommon in untreated myxœdema, rapidly improve, though this is not invariable. It usually takes some weeks or even months for the skin, hair and blood picture to become normal, and in the case of the latter it may be necessary to administer iron in addition to thyroid. There is ample evidence to show that longevity and myxœdema are by no means inconsistent, provided the latter is properly treated.

The aim of treatment in myxœdema is to give a daily dose of thyroid sufficient to rid the patient of symptoms. Nothing is to be gained by raising the metabolic rate to an arbitrary standard of normality if symptoms can be eradicated at a lower level, for elderly hypothyroid patients will often develop undesirable symptoms if their metabolism is raised to normal or only a little over it. The practitioner should not feel that an inability to carry out basal metabolic rate determinations need militate against his successful treatment of hypothyroid states: in adult myxœdema the symptoms of the patient should be his guide, in infantile and juvenile hypothyroidism, when a basal metabolic rate determination would be more valuable, it is usually impracticable, even in hospital. There is no way of determining in advance the *exact* dose of thyroid for an individual case of myxœdema, but the response to thyroid is on the whole less [illegible]

about −20; 60 mg (1 gr) to about −10, 0·1 g ($1\frac{1}{2}$ gr) to about −5, and 0·2 g (3 gr.) to approximately ±0. It will be noted again that the more hypothyroid the patient, the more sensitive he is to thyroid. The majority of patients are free from symptoms, and feel well with a maintenance daily dose of 0·1 to 0·15 g ($1\frac{1}{2}$ to $2\frac{1}{2}$ gr.). It is seldom necessary to give more than 0·2 g. (3 gr) a day. In any case, it is wise to start with a small dose of 60 mg (1 gr) a day, or 30 mg. ($\frac{1}{2}$ gr) when the patient is elderly and suspected of having coronary disease. The dose can be gradually raised at intervals of a month until a satis- [illegible]

[illegible]

common, possibly due in some degree to the hypercholesterolæmia characteristic of the condition, and when the metabolism is raised under treatment, and improvement occurs in the output of the heart, anginal symptoms may occur. The sclerosed coronary vessels may have been adequate to maintain a sufficient blood supply to the sluggish myxœdematous myocardium, but quite inadequate for the brisker circulation induced by thyroid. In such cases the practitioner

has to steer a careful course between the Scylla of myxœdema on the one hand and the Charybdis of angina of effort or left-sided heart failure on the other. When angina is a marked feature he may have to be content to relieve only the grosser symptoms of myxœdema, and to maintain the metabolism at about −20 by the prescription of as little as 30 mg. (½ gr.) of thyroid daily.

HYPERTHYROIDISM

ie to excess secretion of thyr · nodular goitre and in prim primary disease of the thyroid gland itself but may be due to an excessive secretion of thyrotrophin by the anterior pituitary. Whatever be the cause three extremely satisfactory methods are available for the treatment of thyrotoxicosis: (1) antithyroid drugs; (2) iodine and subtotal thyroidectomy; (3) radio-active iodine. At present—according to the type of case encountered—each type of therapy has an important role to play in the management of hyperthyroidism, and it is proposed first of all to describe the technique of each form of treatment and thereafter to discuss which method is likely to prove most suitable in the management of the individual patient.

General Management.—Certain general measures are applicable whichever method of treatment is employed.

Rest—Except in mild cases an initial period of rest is desirable. In moderate cases it is sufficient to arrange that the patient does not rise till after breakfast, has two hours' rest in bed or on a couch after lunch, and retires to bed in the early evening between 7 and 8 p m. In more severe cases rest in bed is essential especially for a week or two at the outset, but unless severe heart failure is

pregnancy in a young woman, or some similar psychological disturbance may be discovered in the course of investigation, and should be dealt with. In many cases the doctor is powerless to interfere in respect of such matters even if they be elucidated; but in others his advice may be invaluable. In the discovery of the cause of the disorder, and in exercising his tact and judgment in its elimination, the family doctor, who enjoys the confidence and trust of his patient, can often render service beyond the scope of the hospital specialist. When the environment at home is obviously at fault, as it so often is in these cases, it is important to advise hospital treatment at the outset, and it may be necessary to prohibit visitors and letters

The attainment of mental rest is facilitated by the use of sedatives, of which one of the most effective and probably the most convenient is phenobarbitone. It should be given in doses of 30 to 60 mg. (½ to 1 gr.) twice or thrice daily, according to the individual tolerance to the sedative, which varies greatly. The

2,500 to 3,000 is desirable The increased calories are most simply obtained by giving additional feeds of fruit juice and glucose, switched egg, milk or proprietary

foods such as Ovaltine or Horlick's, which can be interspersed between the principal meals and given last thing at night.

Increase in weight is always a reassuring and satisfactory sign. It is a sound plan in all cases of thyrotoxicosis, even in those in which symptoms have "cured", to make In active cases an quiescent cases, a in weight of even a few pounds, especially if steadily maintained week by week, is disquieting, and is the signal for a review of the whole treatment of the case.

Septic Foci.—Many cases of thyrotoxicosis are noted to follow acute infections, and this observation has led to debate as to the possible role of sepsis in aggravating the symptoms of the disease. In some patients obvious septic foci are present, particularly in the upper respiratory tract (accessory sinuses, tonsils) or in the teeth (pyorrhœa, apical abscesses). Removal of such foci is frequently advocated as a preliminary to a course of medical treatment, and is

operations in such patients. Pre-operative preparation with antithyroid drugs should therefore be undertaken whenever possible until all hyperthyroid signs and symptoms are well controlled before septic foci are removed. This will usually involve treatment for about two months. In those cases in which treatment by antithyroid drugs or radio-active iodine is contra-indicated the removal of septic foci should be postponed until the thyrotoxic state has been abolished by partial thyroidectomy.

Antithyroid Drugs.—Since 1943, when Astwood first reported his results with the thiourea derivatives, a large number of antithyroid compounds have

If excessive dosage is given, the anterior pituitary, stimulated by the hypothyroid state of the individual, produces thyrotrophic hormone in excess, which results in thyroid hyperplasia. This mechanism may be summarized as follows: Antithyroid substance—→Prevention of iodination of tyrosine—→Lack of thyroid

produce gastric irritation so that on the whole they are less satisfactory drugs.

Propyl thiouracil is said to be less toxic than methyl thiouracil, and evidence is accumulating to suggest that carbimazole is less toxic than propyl thiouracil. In the writer's opinion carbimazole is at present the antithyroid drug of choice.

Dosage.—The prevention of thyroxine synthesis is not an all-or-nothing reaction, and a relationship exists between the dose of antithyroid substance and the degree of hypothyroidism produced. The aim in hyperthyroidism is to

decrease the synthesis of thyroxine to a normal level but not below it, so that the pituitary will not be stimulated to produce thyroid hyperplasia.

Antithyroid drugs are given by the mouth in tablet form. The usual dose of propyl or methyl thiouracil for the first three or four weeks of treatment varies from 0 3 to 0 6 g. a day, depending on the severity of the case. As carbimazole is roughly ten times as powerful as the thiouracil preparations, the equivalent range of dosage will be 30 to 60 mg. a day. As these drugs are rapidly excreted they should be given eight-hourly. Once a significant remission has been produced by this initial treatment the dose is reduced to a maintenance one, since a continuation of the high initial dosage would produce myxœdema and the indirect effect of enlargement of the goitre through overproduction of thyrotrophin from the pituitary. The time required to produce a remission varies from case to case, but with optimal dosage usually takes from three to five

The optimum maintenance dose also varies from case to case. The writer

continue for at least a year.

Clinical Effects.—A normal human subject may be given anti-thyroid drugs for months without producing hypothyroidism or goitre This is to be expected, since the rate of metabolism will remain constant as long as the store of thyroid hormone in the gland is adequate to supply the organism. It is only when the store is exhausted that the decreased rate of hormone synthesis becomes

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no result is observed, but by the end of about a week some subjective improvement occurs, the sweating and flushing of the skin being usually the first symptoms to be ameliorated. Thereafter all the thyrotoxic symptoms steadily recede, the improvement being apparent in from three to five weeks. The objective and measurable signs of thyrotoxicosis parallel the subjective sensations of the patient in their improvement.

The blood cholesterol concentration is low in untreated hyperthyroidism just as it is high in myxœdema On the average it rises under the influence of thiouracil, but it is not a reliable yardstick for the control of treatment since in individual cases there is often little correlation between the blood cholesterol concentration and the progress of the case.

practice and is certainly not one which should be attempted on out-patients

without admitting them to hospital for a night or more if accurate results are to be obtained. Even in hospital many patients become over-anxious about their

from three to five weeks, as experience has shown that the B.M.R. is usually almost normal by this time.

A gain in weight is a characteristic effect of treatment. This generally

pulse pressure. When a severe degree of tachycardia exists its control is often delayed long after the B.M.R. has fallen to normal and the weight and other signs and symptoms have greatly improved. Patience, therefore, has sometimes to be exercised in this respect.

In about 50 per cent of cases auricular fibrillation due to thyrotoxicosis returns to normal rhythm under the influence of the drugs, just as normal rhythm may occur spontaneously after thyroidectomy. In a number of cases, however, the fibrillation persists in spite of satisfactory control of the other features of hyperthyroidism, just as it may persist after thyroidectomy, and quinidine treatment may be necessary following full digitalization to restore the rhythm to normal (see p 598)

The mild diabetic state so commonly associated with thyrotoxicosis may often be cured by the drugs just as it may be cured by thyroidectomy. There are, of course, other thyrotoxic cases with true severe diabetes, and such diabetes is not cured, though it may be ameliorated, by antithyroid drugs or thyroidectomy. In these latter cases dietetic and insulin treatment must be instituted, as described on p 289

The exophthalmos is not usually materially benefited by drug treatment.

treatment in the dosage advised does

Almost invariably the goitre becomes

roduced by iodine Occasionally the

n some cases in which the thyrotoxic

tendency has been abolished and it has been possible to give up the drug alto-

of the goitre will occur. This certainly takes place when a patient is overdosed, and unless care is exercised very large goitres may be produced in this way. An increase in the size of the gland, especially when it is associated with signs and

to very serious toxic reactions. It is most important that the practitioner should be familiar with and be on the lookout for their toxic effects. The recorded signs of toxicity are fever, enlargement of lymph glands and spleen, rashes, conjunctivitis, swelling of the legs and feet, leucopenia, granulopenia, thrombocytopenia and acute sensitivity reactions consisting of high temperature and vomiting Of these the serious *signs calling for a cessation of treatment are the* acute sensitivity reactions and the blood dyscrasias These latter may occur so rapidly that very frequent white blood counts would have to be made in order *to recognize the tendency at an early stage, which is impracticable.* Patients

not such as to make this treatment unsuitable for use in general practice, and

toxic than methyl or even propyl thiouracil, and once the patient is established on a maintenance dose of this drug side-effects are very rare.

Ultimate Effects of Drug Treatment.—Maintenance dosage must be continued for at least a year, for if it is discontinued after a shorter time a gradual return of thyrotoxic signs and symptoms takes place in a high proportion of cases. Further, it is unwise to stop the use of the drug unless it has been found possible to control completely all thyrotoxic signs and symptoms for some months with a maintenance dose of as little as 50 mg. of methyl or propyl

been stopped, it is exceptional for relapse to occur. Most relapses take place within two to four months of stopping treatment. A relapse can, of course, be controlled again by a further course of treatment, but our experience suggests *that if relapse occurs after adequate treatment* a further relapse will probably

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repeated attacks. For the first group a course of treatment with antithyroid drugs is a simple and satisfactory form of therapy and it seems unjustifiable to employ a major *operation for such cases Those who get repeated attacks* can also be re-treated, and there is no doubt that such patients can usually be

means if they are properly supervised. If no

as a satisfactory

cyanocobalamin

in pernicious anæmia. Such treatment, however, becomes somewhat tedious and wearisome to patient and *doctor and alternative methods of treatment* would seem more appropriate for this relapsing type of case It is interesting to note that long ago—before any specific treatment was available—about 50 per cent. of patients suffering from *primary thyrotoxicosis recovered spontaneously* after a longer or shorter time, and it is probable that all we are accomplishing with antithyroid drugs is to maintain such patients in a euthyroid state in the hope that spontaneous recovery *will occur.*

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a year. Fully half the cases will require no further treatment. The remainder will relapse, usually within a few months after finishing treatment, and can then be dealt with by other measures.

Iodine.—The most common alternative to antithyroid drug treatment is partial thyroidectomy.

Both antithyroid drugs and iodine have their advantages and disadvantages in the preparation of patients for thyroidectomy. Iodine seldom restores the metabolism of a severe case to normal, and, though it greatly improves thyrotoxic signs and symptoms, it only ameliorates them to a greater or less extent and does not hold them in complete abeyance as is usually the case with antithyroid drugs. Further, there is a crucial moment to operate upon a patient who has been given iodine—between the tenth and the fourteenth day. If that moment is missed, owing perhaps to the patient developing a respiratory infection, it is necessary to wait for two or three months and to start all over again, for it is dangerous to operate upon a patient when the B.M.R. is on the up-grade. With antithyroid

thyrotoxic signs and symptoms are controlled. Their administration is then stopped and iodine is given for the ten or fourteen days immediately preceding the operation.

familiar Lugol's solution. This contains a mixture of iodine (5 per cent.) and potassium iodide (10 per cent.) in water. The iodine content of potassium iodide

reason for prescribing iodine in this cumbersome form, exactly similar results being obtained by giving potassium iodide in appropriate doses; in fact, the substitution of potassium iodide for Lugol's solution is long overdue. The dosage of potassium iodide required in cases of hyperthyroidism is small by

to very serious toxic reactions. It is most important that the practitioner should be familiar with and be on the lookout for their toxic effects The recorded signs of toxicity are fever, enlargement of lymph glands and spleen, rashes, conjunctivitis, swelling of the legs and feet, leucopenia, granulopenia, thrombocytopenia and acute sensitivity reactions consisting of high temperature and vomiting. Of these the serious signs calling for a cessation of treatment are the acute sensitivity reactions and the blood dyscrasias. These latter may occur so rapidly that very frequent white blood counts would have to be made in order to recognize the tendency at an early stage, which is impracticable. Patients should, therefore, be warned to stop taking the drug and to report to the doctor should any untoward symptoms arise and particularly on the first sign of a sore throat. Provided they do this at once the risk of serious toxic reactions is not such as to make this treatment unsuitable for use in general practice, and when the thyrotoxicosis is mild the patients may be treated successfully from the outset as ambulant cases. The occurrence of toxic reactions tends to diminish the longer the patient has been taking the drug. The treatment of agranulo-

Ultimate Effects of Drug Treatment.—Maintenance dosage must be continued for at least a year, for if it is discontinued after a shorter time a gradual return of thyrotoxic signs and symptoms takes place in a high proportion of cases. Further, it is unwise to stop the use of the drug unless it has been found possible to control completely all thyrotoxic signs and symptoms for some months with a maintenance dose of as little as 50 mg of methyl or propyl

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repeated attacks For the first group a course of treatment with antithyroid drugs is a simple and satisfactory form of therapy and it seems unjustifiable to employ a major operation for such cases. Those who get repeated attacks can also be re-treated, and there is no doubt that such patients can usually be maintained in good health by such means if they are properly supervised. If no alternative treatment were available, this would be regarded as a satisfactory form of therapy comparable to the use of insulin in diabetes or cyanocobalamin in pernicious anæmia. Such treatment, however, becomes somewhat tedious and wearisome to patient and doctor and alternative methods of treatment would seem more appropriate for this relapsing type of case. It is interesting to note that long ago—before any specific treatment was available—about 50 per cent. of patients suffering from primary thyrotoxicosis recovered spontaneously after a longer or shorter time, and it is probable that all we are accomplishing with antithyroid drugs is to maintain such patients in a euthyroid state in the hope that spontaneous recovery will occur.

we are unable to predict the likely behaviour of a hyperthyroid patient at the outset. Under these circumstances the most reasonable procedure is to give, with certain rather numerous exceptions (see p. 367), all cases of primary

be dealt with by other measures.

Iodine.—The most common alternative to antithyroid drug treatment is partial thyroidectomy.

Both antithyroid drugs and iodine have their advantages and disadvantages in the preparation of patients for thyroidectomy. Iodine seldom restores the metabolism of a severe case to normal, and, though it greatly improves thyrotoxic signs and symptoms, it only ameliorates them to a greater or less extent and does not hold them in complete abeyance as is usually the case with antithyroid drugs. Further, there is a crucial moment to operate upon a patient who has been given iodine—between the tenth and the fourteenth day. If that moment is missed,

drugs the effect is permanent as long as the administration of the drug is continued, and any convenient date can be chosen for operation. On the other hand, there seems little doubt that the thyroids of patients prepared for operation by antithyroid drugs are more vascular than those prepared by iodine, and this is greatly disliked by the surgeon. Thus, for those patients who do not show toxic reactions to the drugs, the ideal pre-operative treatment probably involves their use as well as iodine. The drugs are given for a month in full dosage until all thyrotoxic signs and symptoms are controlled. Their administration is then stopped and iodine is given for the ten or fourteen days immediately preceding the operation.

Iodine antagonizes the excessive action of thyrotrophin and causes an increase in the storage of colloid and a decrease in the rate of transfer of thyroxine from the thyroid to the blood. In consequence the signs and symptoms of thyrotoxicosis decrease. Iodine continues to be widely prescribed in the familiar Lugol's solution. This contains a mixture of iodine (5 per cent.) and potassium iodide (10 per cent.) in water. The iodine content of potassium iodide is approximately 75 per cent., so that the total iodine content of Lugol's solution works out at approximately 10 per cent. On this basis 0.6 ml. (10 min.) of the solution contain the equivalent of 60 mg. (1 gr.) of iodine. There seems no valid reason for prescribing iodine in this cumbersome form, exactly similar results being obtained by giving potassium iodide in appropriate doses: in fact, the substitution of potassium iodide for Lugol's solution is long overdue. The dosage of potassium iodide required in cases of hyperthyroidism is small by

potassium iodide in cases of thyrotoxicosis is 60 mg. (1 gr.) twice daily. The

drug may be prescribed conveniently in a solution containing 60 mg. (1 gr.) to 4 ml. (1 fl. dr.) flavoured as desired.

The iodine content of this dose has been shown to be ... in excess ... eful work ... maximum ... ne is contained in about 0 06 ml. (1 min.) of Lugol's solution per day. The larger doses commonly employed do no harm, provided their use does not lead the physician into the fallacy of believing that 6 ml. (90 min) per day will produce a more dramatic effect than 0 3 or 1 ml. (5 or 15 min.) a day.

... appears to exert no influence either on the steepness or the depth of the fall. During this period of falling B.M R. there is a marked decrease in the intensity of all symptoms, with a gain in weight, and a slowing of the pulse rate. This iodine response occurs in the great majority of cases, though now and then a patient fails to react in the classical manner.

Opinions differ as to the course of the disease when iodine administration is prolonged beyond the ten to fourteen day period In general, the opinion of physicians and surgeons is that the pulse and B.M.R. start to rise again, the symptoms become aggravated, and a general deterioration in the patient's health occurs. Such a patient is considered to have escaped from iodine control and to be refractory to further dosage. There is no doubt that such deterioration ...

and it is claimed that such cases may be on the up-grade of a cycle of activity during the period of observation. If iodine be stopped when such a case is growing steadily worse there is a sharp acceleration of the deterioration, which is claimed to represent the escape from iodine control consequent on the cessation of the administration of the drug. Iodine is considered to hold the symptoms and B.M.R in check at a level somewhat below that which they would attain in the uniodized case.

The question of iodine resistance is of considerable practical importance, since pre-operative preparation with iodine is so important There is no doubt that when operation is contemplated the first abrupt fall in the B.M.R., etc., ...

two to three months before operation. At the end of this period iodine refractoriness will have disappeared and the drug may be restarted and operation carried out as in the freshly iodized case. On the other hand, if it is believed that the climbing B.M.R., etc., under iodine does not denote iodine escape but a natural cycle of activity, then the administration of the drug should be continued, secure in the belief that the peak of the crisis will be lessened by its control. Operation may then be carried out when the crisis of the cycle has passed and the metabolic rate is once more upon the down-grade. Evidence at

the moment is not conclusive, but it is safe to say that, in general surgeons prefer freshly iodized cases and will not operate on patients who have taken iodine for prolonged periods unless an iodine-free period of six to eight weeks has elapsed immediately before the pre-operative iodine preparation.

Pre-operative Treatment.—Careful medical preparation is an essential preliminary to operation The patient should if possible be in the hospital or nursing home in which the operation is to be performed, though preferably not in the surgical ward. The date of the proposed operation should be left indefinite to the patient. Rest in bed should be maintained and phenobarbitone or other sedative should be administered. Visitors should be few and every measure taken to ensure that the patient is mentally at ease. A generous diet of the type already described (p. 356) should be allowed, with the addition in the

have fallen to a new low level and the most favourable moment for operation occurs. The general state of the patient leaves no doubt as to the improvement, of which the low pulse rate and B.M.R are merely reflections Estimations of

safe will help to allay the apprehension with which many regard the ordeal.

Thyrotoxic patients suffering from congestive heart failure with auricular fibrillation ideally are treated nowadays with radio-active iodine (see p. 366). When this is not available, the pre-operative treatment of such cases does not differ, so far as the thyrotoxicosis is concerned, from that of an uncomplicated

operation, and should be continued in the post-operative period. It is not good practice to attempt to restore normal rhythm by means of quinidine before operation, for patients so restored often relapse into fibrillation at operation or during the post-operative phase

Immediate Pre-operative Treatment—The patient should be under the influence of a basal narcotic from the early morning of the day of operation. Paraldehyde, given *per rectum*, in a dose of 4 ml. (1 fl. dr.) per stone of body-weight, with a maximum of 28 ml. (8 fl. dr), is generally effective and can be

drug may be prescribed conveniently in a solution containing 60 mg. (1 gr.) to 4 ml. (1 fl. dr.) flavoured as desired.

The iodine content of this dose has been shown to be considerably in excess of the quantity required for full iodine effect. It appears from the ...
of Means, Lerman and ...
effect on pulse rate, B ...
tained in about 0·06 ml. (1 min.) of Lugol's solution per day. The larger doses ...

appears to exert no influence either on the steepness or the depth of the fall. During this period of falling B.M.R. there is a marked decrease in the intensity of all symptoms, with a gain in weight, and a slowing of the pulse rate. This iodine response occurs in the great majority of cases, though now and then a patient fails to react in the classical manner.

Opinions differ as to the course of the disease when iodine administration is prolonged beyond the ten to fourteen day period. In general, the opinion of physicians and surgeons is that the pulse and B.M.R. start to rise again, the symptoms become aggravated, and a general deterioration in the patient's health occurs. Such a patient is considered to have escaped from iodine control and to be refractory to further dosage. There is no doubt that such deterioration under iodine usually occurs in patients allowed to go on taking the drug after the first ten to fourteen days. Means and Lerman, however, consider that such patients are not really iodine resistant, but are still under the control of iodine though their state grows worse. The disease is known to pursue a cyclic course, and it is claimed that such cases may be on the up-grade of a cycle of activity during the period of observation. If iodine be stopped when such a case is growing steadily worse there is a sharp acceleration of the deterioration, which is claimed to represent the escape from iodine control consequent on the cessation of the administration of the drug. Iodine is considered to hold the symptoms and B.M.R. in check at a level somewhat below that which they would attain in the uniodized case.

The question of iodine resistance is of considerable practical importance, since pre-operative preparation with iodine is so important. There is no doubt that when operation is contemplated the first abrupt fall in the B.M.R., etc., ...

imaginary, then the patient should be sent away *without* iodine for a period of two to three months before operation. At the end of this period iodine refractoriness will have disappeared and the drug may be restarted and operation carried out as in the freshly iodized case. On the other hand, if it is believed that the climbing B.M.R., etc., under iodine does not denote iodine escape but a natural cycle of activity, then the administration of the drug should be continued, secure in the belief that the peak of the crisis will be lessened by its control. Operation may then be carried out when the crisis of the cycle has passed and the metabolic rate is once more upon the down-grade. Evidence at

and great restlessness of the patient presenting an unforgettable clinical picture. The condition, once it has developed, is very intractable and is attended by a high death-rate. The essence of its treatment is in its *prevention*. It should very rarely occur after operation in cases properly treated pre-operatively and in which the time of operation has been well selected. Nor should it occur in well-supervised medical cases, for it is seldom that a case of moderate severity suddenly goes into crisis It arises usually in those patients who have been deteriorating for some time, or who have run a severe course for months or years, and who therefore have not had timely and efficient treatment. It frequently occurs in cases of moderate or severe toxicity who have drifted out of medical supervision, and in the writer's experience has been more common in such " medical " cases than after thyroidectomy. It may also occur, with fatal results, after ill-timed operations for focal sepsis (tonsillectomy, etc.) in moderately toxic patients

Established cases of hyperthyroid crisis should be treated on the lines detailed for the management of patients after thyroidectomy. Quiet and seclusion with adequate morphine are essentials The promotion of heat loss and avoidance of hyperpyrexia can be aided by tepid sponging or, in more desperate

(one pint) every sixty minutes. Iodine can be given as 0 3 to 0 6 g. (5 to 10 gr.) of potassium iodide in the intravenous saline. It is useless to employ antithyroid drugs in hyperthyroid crisis owing to the number of days which must elapse before such treatment produces its effect

appears less efficacious than in auricular fibrillation of other ætiology.

Tetany and Vocal Cord Paralysis.—With modern surgical technique these complications are now rare except in the case of a second operation undertaken because of a recurrence of thyrotoxicosis Recurrent thyrotoxicosis should, therefore, be treated by antithyroid drugs or preferably by radio-active iodine (see p. 366) The treatment of hypoparathyroidism is dealt with on p. 369

Hæmorrhage.—While the treatment of post-operative hæmorrhage must remain a surgical problem, it is necessary for the physician who may be looking after the patient to recognize the indications for calling surgical aid. It is seldom that massive hæmorrhage occurs, with the symptoms of collapse, due to blood loss. Much more commonly hæmorrhage into the wound causes local tension and may result in symptoms from pressure on the trachea. It should be remembered that oozing of serous fluid frequently occurs and may cause

operation and is more common in male than in female cases, especially in those in whom exophthalmos has been a prominent feature of the thyrotoxicosis. In

asleep before the anæsthetic is started. In no case should operation be attempted if the patient is acutely conscious and distressed or if the pulse rate on the table rises to 130 or more. It is wiser to postpone the operation for a day or two than to risk a post-operative thyrotoxic crisis.

Post-operative Treatment.—The critical stormy period occurs in the first forty-eight hours after the operation During this period the patient should be nursed in absolute quiet and seclusion, either in a room by herself or screened off in a corner of a general ward. Visitors and letters should be forbidden and medical examinations reduced to a minimum. It is desirable that one day and [illegible] k should have charge [illegible] record of pulse and

Owing to the high metabolism after the operation the temperature rises in most cases and few bedclothes are necessary or desirable. Heat loss is facilitated by cool air and light coverings, and chills are very rare. Quiet is assured by *hypodermic administration of morphine*, which is repeated as required.

The administration of adequate amounts of fluids is most important, and, if the patient is dehydrated or unable to swallow, an intravenous drip transfusion of 5 per cent. glucose in saline should be started at once and continued till the patient is able to take fluids by the mouth. Glucose and orange drinks by mouth may then be substituted or used as adjuvants.

Iodine is frequently given post-operatively, potassium iodide being added to the intravenous infusion in doses of 0 3 to 0 6 g. (5 to 10 gr.) If the patient has been thoroughly iodized before operation, this is less necessary, but, once the patient is able to swallow, it is usual to continue iodine in the same dosage as in the pre-operative period for a week

In many cases soreness of the throat is a troublesome post-operative feature. This is best controlled by steam inhalations, rest to the voice and sedatives. A watch must be kept for the occurrence of post-operative complications—crisis, tetany or hæmorrhage. These demand special treatment, to be considered below.

In an uncomplicated case such measures are sufficient to carry the patient over to the third or fourth day, when rapid improvement has as a rule been [illegible]

stitches are removed on the fourth or fifth day, and in most cases the patient is fit to get up for a short period within a few days of operation, though severe reaction, or the presence of cardiac failure, may delay progress considerably. [illegible] nths advised

[illegible] may occur post-operatively, or may supervene at any time in severe cases under medical treatment Its occurrence is usually a reflection on the efficiency of the medical control of the case. A common precipitating factor is a pulmonary infection. In all cases its recognition is only too easy—the high fever, extreme tachycardia

[illegible]

ment so far encountered is myxœdema, which occurs in up to 10 per cent. of cases treated, particularly when the attempt is made to control the disease with a single dose of ^{131}I. Most patients who are going to develop myxœdema do so within three to five months after receiving ^{131}I. Transient myxœdema is much more common. The B.M.R frequently falls to subnormal levels some two or three months after therapy, rebounding after a shorter or longer time to normality. The phenomenon may be due either to temporary damage to some of the thyroid cells or to ultimate hypertrophy or hyperplasia of the remainder.

Although considerable improvement may be observed within a month after the patient has received the dose of ^{131}I, this may not be maximal for two or three months Thus there may be a considerable time-lag between the giving of the dose and the attainment of a euthyroid state. In seriously thyrotoxic cases, therefore, and especially in patients showing signs of cardiac decompensation, it seems wise to use this form of treatment only after at least partial euthyroidism has been attained by the use of antithyroid drugs

Treatment with ^{131}I is extremely simple for the patient and brings about a [illegible]

surgery.

The dose of ^{131}I will vary enormously from patient to patient and depends on a large number of factors—particularly the severity of the thyrotoxicosis and the size and nodularity of the thyroid By using a tracer dose it is possible to calculate the theoretical therapeutic requirements of ^{131}I by measuring the uptake of the tracer dose by the thyroid, the rate of its elimination from the gland and by attempting to assess the volume of gland tissue to be irradiated. Experience has shown, however, that these techniques have not yielded results greatly superior to those based on a clinical evaluation of the type of gland to be dealt with and the clinical condition of the patient. The estimation of the dose required, however, is a specialized procedure requiring considerable experience and is beyond the scope of this book.

Choice of Treatment.—The selection of the most desirable method of treatment in any patient suffering from thyrotoxicosis is best approached by considering the problem in two phases Firstly, there is the need to control the hyperthyroid state for which treatment with antithyroid drugs is most suitable. Thereafter definitive treatment becomes the major objective—either the prolonged use of antithyroid drugs, sub-total thyroidectomy following a short course of iodine, or the administration of ^{131}I Each method of therapy has certain advantages and disadvantages, and the significance of these vary with the problems of the individual patient Nevertheless, it may be helpful to make some broad generalizations which may aid the practitioner in his choice.

Indications for Antithyroid Drug Treatment.—Antithyroid drugs are the treatment of choice for the rare cases of thyrotoxicosis which occur in children or at puberty. The disturbance in such patients is usually self-limiting and it is only necessary to maintain the patient in a euthyroid state till spontaneous remission occurs. The drugs are also indicated when hyperthyroidism occurs

such patients, therefore, thyroidectomy is an unwise procedure unless there are pressing reasons to the contrary. This form of exophthalmos may, of course, arise quite independently of thyroidectomy and may even occur in patients in whom there has never been any sign of thyrotoxicosis. Its exact cause is still obscure. It is probably due either to an excess secretion of thyrotrophin or to an exophthalmic factor from the anterior pituitary, causing œdema of the lids and retro-orbital tissues with an increase in the amount of fat in the orbital fossa. In addition to exophthalmos there is mechanical interference with the extrinsic muscles of the eye, giving rise to double vision and difficulty in ocular movements. In a few cases the exophthalmos may become so pronounced as to make the closure of the eyes impossible, leading to exposure keratitis and even blindness. In such cases it is necessary to consult an ophthalmologist, who may advise lateral tarsorrhaphy or in extreme cases orbital decompression. In less urgent cases medical treatment is directed to the inhibition of the production of the offending hormone from the anterior pituitary. All the hormones, which the

and obvious difficulties arise when thyrotoxicosis complicates the exophthalmos,

the writer's experience remission has most commonly followed the skilled irradiation of the retro-orbital tissues.

Myxœdema.—Cases of myxœdema arising after thyroidectomy must be treated with thyroid extract. The treatment does not differ from that in cases of myxœdema of other ætiology and should be along the lines suggested on p. 354.

Radioactive Iodine.—Some thirty years ago radiation by X-rays or radium was used very extensively in the treatment of hyperthyroidism. General dissatisfaction with the results and the striking success of surgical treatment led to an abandonment of this form of treatment. Before the introduction of anti- ... and with the modern ... proportion of cases ... ce more superseded radiation in the therapy of thyrotoxicosis. Now radiation again occupies an important place in the treatment of hyperthyroidism, but this time the radiation is effected not by deep X-ray therapy or by radium but by an isotope of iodine. The radio-active isotope of iodine, ^{131}I, with a half-life of eight days, has been the most effective of all isotopes used therapeutically because of iodine's singular propensity to concentrate in the thyroid gland to an extent about 10,000 times greater than in any other organ. It is therefore taken up with particular avidity by the hyperthyroid gland where the ionising radiations produce subsequent destruction and fibrosis. The resultant depression of function of the thyroid is proportional to the total uptake of the isotope and the size of the therapeutic dose. [illegible] malignant changes [illegible] pursued very ginge. [illegible]

ever, suggests that such fears are unjustified, though the possibility of the development of late malignant changes in fifteen to twenty years in patients so treated has not yet been entirely excluded. The only major complication of this treatment so far encountered is myxœdema, which occurs in up to 10 per cent. of cases treated, particularly when the attempt is made to control the disease with a single dose of ^{131}I. Most patients who are going to develop myxœdema do so within three to five months after receiving ^{131}I. Transient myxœdema is much more common. The B.M.R. frequently falls to subnormal levels some two or three months after therapy, rebounding after a shorter or longer time to normality. The phenomenon may be due either to temporary damage to some of the thyroid cells or to ultimate hypertrophy or hyperplasia of the remainder.

Although considerable improvement may be observed within a month after the patient has received the dose of ^{131}I, this may not be maximal for two or three months. Thus there may be a considerable time-lag between the giving of the dose and the attainment of a euthyroid state. In seriously thyrotoxic cases, therefore, and especially in patients showing signs of cardiac decompensation, it seems wise to use this form of treatment only after at least partial euthyroidism has been attained by the use of antithyroid drugs.

Treatment with ^{131}I is extremely simple for the patient and brings about a euthyroid state in a large proportion of cases without an operation or prolonged drug therapy. Nevertheless, it demands special facilities in properly equipped centres so that it is not as yet as universally available as antithyroid drugs or surgery.

The dose of ^{131}I will vary enormously from patient to patient and depends on a large number of factors—particularly the severity of the thyrotoxicosis and the size and nodularity of the thyroid. By using a tracer dose it is possible to calculate the theoretical therapeutic requirements of ^{131}I by measuring the uptake of the tracer dose by the thyroid, the rate of its elimination from the gland and by attempting to assess the volume of gland tissue to be irradiated. Experience has shown, however, that these techniques have not yielded results greatly superior to those based on a clinical evaluation of the type of gland to be dealt with and the clinical condition of the patient. The estimation of the dose required, however, is a specialized procedure requiring considerable experience and is beyond the scope of this book.

Choice of Treatment.—The selection of the most desirable method of treatment in any patient suffering from thyrotoxicosis is best approached by considering the problem in two phases. Firstly, there is the need to control the hyperthyroid state for which treatment with antithyroid drugs is most suitable. Thereafter definitive treatment becomes the major objective—either the prolonged use of antithyroid drugs, sub-total thyroidectomy following a short course of iodine, or the administration of ^{131}I. Each method of therapy has certain advantages and disadvantages, and the significance of these vary with the problems of the individual patient. Nevertheless, it may be helpful to make some broad generalizations which may aid the practitioner in his choice.

Indications for Antithyroid Drug Treatment.—Antithyroid drugs are the treatment of choice for the rare cases of thyrotoxicosis which occur in children or at puberty. The disturbance in such patients is usually self-limiting and it is only necessary to maintain the patient in a euthyroid state till spontaneous remission occurs. The drugs are also indicated when hyperthyroidism occurs

during pregnancy. Surgery is undesirable in late pregnancy and radio-active iodine treatment is absolutely contra-indicated. Most patients can be maintained in a euthyroid state during pregnancy and the puerperium by carefully graded dosage, but as the drugs are secreted in the milk the patient should not be allowed to nurse her baby. The danger that the function of the fœtal thyroid may be depressed by the drugs and, owing to their goitrogenic action, that the child may be born with a goitre, is not in our experience a very serious one provided care is taken not to cause hypothyroidism in the mother by overdosage. Lastly, antithyroid drugs are indicated for the large group of young women with moderate primary Graves' disease and unobtrusive goitres who usually react satisfactorily to them and often obtain a permanent remission. The idea of an irrevocable radical interference with the endocrine system in such cases is repugnant if it can be avoided, and it is always possible to resort to surgery if drug treatment fails.

Indications for Surgery.—Patients who relapse following an adequate course of antithyroid drugs should be operated upon, since if they relapse once they will probably relapse again after a second course. Surgery is also indicated for those who develop serious toxic reactions to the drugs, and for patients with large unsightly goitres or goitres causing pressure symptoms. Some patients are so unreliable and unco-operative that they must be relieved of responsibility for their own cure by surgery. Lastly, patients between the ages of thirty-five and forty-five with nodular goitres are usually best treated by subtotal thyroidectomy. The possibility of malignant degeneration occurring in a thyrotoxic adenoma is sometimes mentioned as an argument in favour of thyroidectomy in such cases. Malignant change, however, practically never occurs in thyrotoxic glands, and this should not be regarded as a significant factor in deciding upon thyroidectomy.

Indications for Treatment with ^{131}I. Radio-active iodine therapy may prove in time to be the treatment of choice for the majority of cases of thyrotoxicosis. Nevertheless, until it is quite certain that such treatment will not produce late malignant changes in the thyroid and in view of the possible genetic effects of the isotope, it is wise to be conservative and to limit the use of ^{131}I to patients over the age of forty-five for whom it is the treatment of choice. It should also be employed for all patients who develop recurrent thyrotoxicosis following thyroidectomy owing to the considerable risk of a second operation causing vocal cord paralysis or hypoparathyroidism in such patients, and for toxic retrosternal goitre. Lastly, it is preferable for those in whom severe exoph-
[illegible] eloping
d, any
cularly

Individual Indications.—The clinical types in which either antithyroid drugs, surgery or radio-active iodine are definitely the treatment of choice have been indicated. There remains, however, a large number of patients who do not conform to these definite types, and in whom it is best not to adhere to any rigid rule but rather to treat each patient as an individual problem according to the circumstances of the case. These vary widely, and the type of therapy selected

long ceased to worry about her personal appearance, but one of shattering concern to a pretty girl. Since there is great variation in the number and significance of these factors, dogmatic generalizations are undesirable. Some of the factors deserving attention in the selection of therapy are presented in the following table:

FACTORS INFLUENCING CHOICE OF TREATMENT IN THYROTOXICOSIS

	Thyroidectomy	*Antithyroid Drug*	^{131}I
Age over forty-five	—	—	Yes
Recent and acute in young	—	Yes	—
Relapse after antithyroid drugs	Yes	—	Yes
Previous operation	—	—	Yes
No hypoparathyroidism and vocal paralysis	—	Yes	Yes
Auricular fibrillation	—	—	Yes
Congestive failure	—	—	Yes
Large gland	Yes	—	Yes
Pressure symptoms	Yes	—	Yes
Exophthalmos	—	Yes	Yes
Pregnancy		Yes	—
Safety		—	Yes
Permanence of cure	Yes	—	Yes
Rapidity of cure	Yes	—	—
General availability	—	Yes	—
Less immediate time lost from work	—	Yes	Yes
No scarring	—	Yes	Yes
No permanent myxœdema	—	Yes	—
No acute emotional upset	—	Yes	Yes
No chronic emotional upset	Yes	—	Yes

THE PARATHYROID GLANDS

HYPOPARATHYROIDISM

This condition may result from a parathyroidectomy undertaken for hyperparathyroidism, from a total or subtotal thyroidectomy, or may occasionally arise spontaneously for no apparent cause. The symptoms, which may become manifest as early as twenty-four hours after the operation or may be delayed in their onset for a week, rapidly become serious and demand urgent treatment. If carpo-pedal spasm or laryngismus is already apparent when the patient is seen, an intravenous injection of calcium gluconate should immediately be given. Ten to twenty ml. of a 10 per cent solution should be injected very slowly intravenously, five minutes being allowed for the injection. The injection causes an almost immediate disappearance of the symptoms of tetany. The whole procedure may have to be repeated several times if the symptoms reappear, which will probably be necessary as the total amount of calcium given in this

way is exceedingly small (10 ml. of a 10 per cent. solution of calcium gluconate contains only 89 mg. of calcium).

It is wise, *however, to begin parathyroid or vitamin D medication* as soon as possible. Recent work has shown that the latter is the more efficient because the effect of parathyroid extract rapidly diminishes owing to the development of an anti-hormone; it is also very costly. If there is an indication for therapy with parathyroid extract it is at the onset of tetany when an intramuscular injection of 20 to 60 units (2 to 3 ml.) depending on the severity of the case, will produce a rise in serum calcium which begins within six hours and is maintained for about eighteen hours. The initial dose can be repeated every six hours provided a careful watch is kept on the level of the serum calcium, which should not exceed 13 mg. per 100 ml. Tetany following removal of a parathyroid *tumour does not generally last longer than two or three days, after which time* the remaining parathyroid tissue is usually capable of producing a sufficiency of hormone. It is in this type of case that intramuscular injections of parathyroid extract may effectively tide over the period of hypocalcæmia until the endogenous secretion of hormone has reached a satisfactory level. When, however, the condition has resulted from thyroidectomy there may be little or no parathyroid tissue left in the body, in which case vitamin D therapy is much more satisfactory. It not only increases the absorption of calcium from the gastro-intestinal tract but also facilitates the excretion of phosphorus in the urine. Dihydrotachysterol (AT 10), a derivative of irradiated ergosterol and therefore *closely allied to vitamin D, has the reputation of being more effective than* vitamin D.

containing 5

9 mg. per 10

dosage, however, should be controlled by a rough estimation of the amount of calcium being excreted in a twenty-four-hours' specimen of urine, which may be done very simply by the use of Sulkowitch's test.[1] If a marked turbidity appears in the urine on applying this test, the dosage should be reduced. Vitamin D in oral doses of 1 to 5 mg. of calciferol (equivalent to 40,000-200,000 international units of vitamin D) has been shown to be almost as effective in *raising the serum calcium level, and in view of its greater* availability and much smaller cost should undoubtedly be used for maintenance treatment. Occasionally it may be necessary to use much larger doses. In one instance daily doses of 500,000 units were given for fifty days, resulting in an increase of serum calcium and the disappearance of symptoms, the patient remaining well for at [illegible] without further treatment. Tablets of high-potency calciferol

Each tablet contains

e *crystalline* calciferol.

n gives rise to severe

intolerance when patients are observed adequately during treatment and taught to test the urine regularly by the Sulkowitch test. This will give a much earlier warning of hypercalcæmia than the more elaborate and time-consuming determination of the serum calcium.

[1] Sulkowitch's Test.—The reagent is made as follows. 2·5 g. of oxalic acid, 2·5 g. of [illegible] ed in distilled water and the *volume* [illegible]

Milk and cheese, in spite of being rich in calcium, are contra-indicated because of their high phosphorus content. Other foods rich in phosphorus such as egg-yolk and cauliflower should also be omitted. Phosphate absorption from the alimentary tract can be diminished by giving 1 to 2 tablespoonfuls of aluminium hydroxide gel three times a day with meals and the calcium intake increased by the administration of 1 g. of calcium lactate three or four times a day.

HYPERPARATHYROIDISM

The clinical picture designated as generalized fibro-cystic osteitis is the result of overaction of the parathyroid glands. It is characterized by pains in the limbs and fractures; occasionally attention is drawn to the condition by renal colic produced by calculi in the urinary tract, the formation of which frequently precedes generalized fibro-cystic osteitis. It is now, indeed, recognized that hyperparathyroidism is a more common aetiological factor in the formation of renal calculi than used to be supposed. X-ray examination may reveal the presence of multiple cystic tumours of the bones, especially the long bones. Biochemical examination of the blood is essential in differentiating this disease from other pathological conditions of the bones such as focal osteitis fibrosa. In the generalized form the serum calcium is usually high, the serum phosphorus low and the plasma alkaline phosphatase greatly increased. These findings are important as indications of hypersecretion of the parathyroid hormone. Should they be present, an exploratory operation should be performed in the hope of removing a parathyroid adenoma. The simple clinical examination of the neck seldom reveals the presence of a tumour, and even at operation its detection may be exceedingly difficult.

The post-operative treatment is carried out on general lines, but a careful watch must be kept for early symptoms of tetany. Should these make their appearance, the intensive treatment described above for post-operative tetany must be instituted.

The results of surgical treatment of generalized fibro-cystic osteitis are good provided renal calcification or infection have not already reached the point where uraemia is inevitable. Very soon the pains in the limbs disappear, and there is a great improvement in health with disappearance of skeletal and urinary symptoms. Naturally it takes very much longer for the bones to recover their normal texture, and months may elapse before there is much reduction of the plasma phosphatase. This emphasizes the necessity for a high calcium intake with abundance of vitamin D.

THE SUPRARENAL GLANDS

ADDISON'S DISEASE

Addison's disease is the result of deficiency of the adrenal cortical hormones. The condition is characterized by an excessive loss of sodium and water in the urine while potassium is retained in the tissues and blood, and by a marked tendency to hypoglycaemia. In association with these changes in body chemistry, concentration of the blood occurs with a diminution in plasma volume. In addition there is an increased sensitivity to noxious stresses of all kinds. Treatment should aim at redressing these disturbances and now depends for the most part on suitable hormonal replacement therapy.

Before the introduction of modern therapeutic measures the disease progressed inexorably to a fatal issue in periods of time varying from a few weeks to not much more than two years. Since the introduction of potent substitution therapy the prognosis has greatly improved, though the life of a patient with Addison's disease is still somewhat precarious owing to the liability of Addisonian crisis, which may be precipitated by intercurrent infections, sometimes of a trivial nature, or by the administration of drugs such as morphine or anæsthetics to which patients with Addison's disease are notoriously intolerant. Such crises, which usually occur very suddenly, are characterized by a high temperature, intractable vomiting, delirium, severe dehydration, hypoglycæmia and shock. In managing a case of Addison's disease the practitioner should seek to prevent crises by increasing substitution therapy on the first sign of an intercurrent infection, and by avoiding the use of general anæsthetics particularly chloroform and ether, the opiates, hypnotics and potassium salts.

Treatment in Crisis.—In Addisonian crisis treatment consists in the administration of large doses of hydrocortisone and deoxycortone acetate (DCA) and in combating shock, dehydration, hypoglycæmia and sodium depletion by warmth a[illegible]
solution
twenty-fou
response As the crisis is often precipitated by a bacterial infection it may be

ient's
-four
hours. It should be added to the intravenous infusion in doses of 100 mg. every six to eight hours, the dose being appropriately reduced later as the patient improves This treatment should be supplemented by intramuscular injections of 10 mg. of DCA two or three times in the first twenty-four hours. Sufficient hormonal treatment and glucose saline should be given to maintain the patient's blood pressure at a level above 100 mm. Hg., but, on the other hand, care must be taken to avoid inducing pulmonary and peripheral œdema.

Maintenance Treatment.—The introduction of cortisone has entirely changed the outlook in Addison's disease. It effectively abolishes the hypoglycæmia, lack of appetite, anæmia and inability to resist stress which characterize the condition Cortisone is not only life-saving but enables the patient to live a full and active life with a well-being little short of that enjoyed by normal individuals. For maintenance purposes the dose varies from 12 5 to 37 5 mg. a day (½ to 1½ tablets). In the presence of active tuberculosis it should be kept as low as possible. Replacement doses of this size never give rise to the undesirable side-effects observed in other conditions in which the drug is given in much larger doses to produce hypercorticism. On the other hand doses of this order are usually insufficient to restore completely the sodium depletion of Addison's disease and to maintain the body fluids and blood pressure at a normal level. The administration of larger doses or the addition to the diet of 10 g. of sodium chloride a day will have this effect, but in the writer's opinion the supplementary use of DCA with a normal sodium intake is usually the preferable treatment. DCA has a powerful effect in conserving sodium chloride and water but has no demonstrable effect in maintaining normal carbohydrate metabolism. The combination of cortisone and DCA, therefore, provides the most satisfactory form of substitution therapy

in Addison's disease. DCA can be given intramuscularly dissolved in ethyl oleate, and when a patient with Addison's disease is first encountered injections of 5 mg. twice or thrice a week should be given in this way till maximum improvement has resulted, after which implantation of pellets of DCA should be made as this is the most economical, effective and least troublesome method of administering the drug. 200 or 300 mg. in the form of pellets—each containing 100 mg.—are inserted into the deep subcutaneous tissues of the abdomen through a small incision which can be closed by a couple of stitches. There is a tendency for such pellets to be extruded in the course of time if they are implanted too superficially or if the edges of the little wound are not carefully undermined and the pellets tucked into pockets well away from the line of the incision by a blunt trocar and cannula made specially for the purpose. If these precautions are undertaken it is most exceptional for pellets to be lost in this way. The effect of DCA thus implanted can be maintained for periods of time varying from five to ten months without the necessity of frequent oily intramuscular injections. An appraisal of the patient's subjective symptoms, his blood pressure, blood chemistry and weight should indicate when a further implantation is becoming necessary.

Fully 50 per cent. of cases of Addison's disease are due to tuberculosis, and active tuberculous disease in other parts of the body, particularly in the lungs, bones and genito-urinary tract, must not be overlooked and when present must receive appropriate treatment. Theoretically cortisone is contra-indicated in the presence of active tuberculous disease, but in practice the small doses necessary for the maintenance treatment of Addison's disease, which simply replace the patient's lost endogenous secretion, are harmless

ADRENAL APOPLEXY

(*Waterhouse-Friderichsen Syndrome*)

In the course of fulminating purpuras and septicæmias—particularly acute meningococcal septicæmia—hæmorrhage may occur into the adrenals. The resulting disease, characterized by shock, abdominal pain, intense purple cyanosis, ecchymotic hæmorrhages and an extremely low blood pressure, presents an unforgettable clinical picture. The patient speedily relapses into unconsciousness and a fatal issue, sometimes within a few hours, was almost invariable before the introduction of hydrocortisone

Energetic treatment may now save life. Apart from the control of the associated septicæmia with antibiotics, treatment with large doses of hydrocortisone, DCA and an intravenous-drip transfusion of 5 per cent. glucose solution in saline is the same as for severe Addisonian crisis

ADRENAL CORTICAL HYPERFUNCTION

Cushing's Syndrome.—Hyperactivity of the adrenal cortex causing excessive quantities of steroids with hydrocortisone-like activity to be produced results in the characteristic signs and symptoms of Cushing's syndrome. This may be due either to hyperplasia of both adrenals or to a benign or malignant tumour of one of them with consequent atrophy of the other. It is usually possible to distinguish between the two conditions by studying the excretion of adrenal steroids in the urine or by radiographic examination following the presacral introduction of oxygen into the peri-renal space.

When the diagnostic procedures indicate the presence of an adrenal tumour it should be removed if obvious metastases are not present. As the contralateral adrenal is nearly always atrophic and practically devoid of endocrine function, acute—and probably fatal—adreno-cortical insufficiency will result unless careful therapy with cortisone is undertaken before, during and after the operation (see p. 91). The administration of cortisone is gradually reduced [illegible]

tinued for three or four weeks in gradually decreasing doses. In a few cases no response occurs owing to the irreversible atrophy of the gland, and substitution therapy with cortisone and DCA, as in the maintenance treatment of Addison's disease, will have to be continued for life. The results of surgical removal of adenomata, given adequate pre- and post-operative treatment, are dramatically successful, but the prognosis in carcinomata is poor as metastases to the lungs and liver usually occur early.

When Cushing's syndrome is due to bilateral adrenal hyperplasia, total adrenalectomy is the treatment of choice. It was Cushing's original opinion that this condition resulted from a tumour of the basophil cells of the anterior pituitary, and there is much evidence to suggest that the adrenal hyperplasia is indeed due to excessive secretion of corticotrophin. Nevertheless, the mortality and complications following hypophysectomy are greater than with bilateral adrenalectomy, and radiation of the pituitary has on the whole given very disappointing results. The results of subtotal adrenalectomy are likewise uncertain. Pre- and post-operative treatment with cortisone (see p. 91) and the careful correction of dehydration and electrolyte disturbances are, of course, essentials of success in total adrenalectomy. The ultimate maintenance treatment is the same as for Addison's disease Convalescence following operation is slow and patients usually experience much mental depression, inertia and obscure gastro-intestinal symptoms for many weeks. A high protein diet, 4 g. of potassium chloride daily and an intramuscular injection of 25 mg of testosterone propionate three times a week, will hasten the recovery phase. Owing to the associated osteoporosis, orthopædic supports to the spine may be necessary.

The Adreno-genital Syndrome.—When adreno-cortical hyperplasia, [illegible]

phroditism and in males macrogenitosomia praecox; (2) before puberty, sexual precocity with coincident masculine change in the female; (3) at or after puberty, virilism

In congenital adrenal hyperplasia the best results are obtained by suppressive [illegible]

If a tumour is not present, the suppressive therapy as for congenital adrenal hyperplasia may be employed with success.

Bilateral hypertrophy of the adrenal cortex causing the adreno-genital syndrome in the adult may also be strikingly improved by suppressive treatment with intramuscular cortisone, the dose being adjusted to reduce the 17-ketosteroid secretion in the urine to below 8 mg. in the twenty-four hours. When

the adreno-genital syndrome is due to an adenoma or adenocarcinoma, or when a mixed picture of Cushing's syndrome and virilism exists, the treatment is surgical, with subsequent replacement therapy as described for Cushing's syndrome (see p. 373). In the absence of malignancy the results of treatment are good and the signs of virilism disappear in the course of a year, though the deepened voice persists as the organic changes in the larynx are permanent.

TUMOURS OF THE ADRENAL MEDULLA

Neuroblastomata of the adrenal medulla are extremely malignant tumours which are practically never diagnosed in time to permit of their successful removal

Hyperfunctioning tumours of the adrenal medulla of chromaffin tissue—*phaeochromocytomata*—result in the condition of paroxysmal hypertension. Such tumours are adenomatous and usually benign. They produce their effects by discharging pathological quantities of adrenaline and noradrenaline into the blood. This rare condition eventually results in degenerative changes [illegible]

THE PITUITARY GLAND

DIABETES INSIPIDUS

Diabetes insipidus, characterized by marked polyuria and thirst, is generally attributed to a lesion in the floor of the third ventricle anterior to the tuber cinereum or to one in the anterior hypothalamus, an extension of which forms the posterior part of the pituitary. The nature of the lesion varies in different patients and may be the result of syphilis, neoplasm, trauma or encephalitis, while there is a group of patients in whom there appears to be a hereditary or familial tendency The condition is closely simulated by a hysterical polydipsia.

If there is evidence of syphilis, vigorous anti-luetic treatment should be instituted. A neoplasm causing this lesion is at present almost always inaccessible to surgical treatment, although deep X-ray therapy sometimes yields promising results. In most cases treatment should be directed to the relief of the thirst and polyuria For this purpose intramuscular injections of vasopressin or preferably a suspension of the pressor fraction in oil (pitressin tannate, Parke, Davis & Co) are of value. Care must be taken to shake the suspension thoroughly before it is injected intramuscularly. Dosage varies from case to case and at different times in the same patient. An average dose will consist of 0 5 ml. of pitressin tannate injected just before bedtime on alternate days, and this may be reduced or increased as the results demand. The salt intake should be restricted, as salt exacerbates the polydipsia. The patient's ability to lead a normal life by day and night is the test of satisfactory control.

It is worth noting that most of the unpleasant reactions such as intestinal colic, nausea and vomiting which may occur after vasopressin do not appear to follow injections of the tannate. With the dose which is here recommended it is very unlikely that the retention of water will be excessive. This is character-

ized by mental confusion, poor muscle co-ordination, headache, nausea and vomiting.

When, for one reason or another, repeated injections are impracticable, an effective, but less satisfactory, *alternative is the snuffing of a pinch of posterior* pituitary powder every four to eight hours. Capsules of such powder may be obtained, each containing 45 mg. of the active principle, and the contents of one capsule snuffed into the nose is usually effective.

The posterior pituitary hormone increases tubular reabsorption of water in the kidney This leads to an increase in the specific gravity of the urine and marked diminution in urinary volume, with consequent retention of water in the tissues and alleviation of thirst. A fluid intake and output almost within normal limits is generally achieved within a few days of the start of pitressin medication.

ADENOMATA OF THE PITUITARY

[illegible]

*symptoms and signs produced depend upon the pressure exerted on the remain-*ing tissue of the anterior lobe and the surrounding structures, upon the extent of actual destruction and the nature of the secretion produced by the tumour cells.

The Chromophobe Adenomata.—A tumour of the chromophobe cells, to which no secretory function has yet been attributed, manifests itself by the effects of pressure on and destruction of pituitary tissue and such structures as the optic chiasma and hypothalamus. The only treatment which holds out any hope is surgical removal, since the chromophobe cells do not appear to be sensitive to X-rays. Increasing loss of eyesight is an important indication for surgical interference, which should be attempted as soon as possible before the destruction of tissue is advanced. Signs of hypopituitarism not infrequently follow the removal of such tumours or may result from pressure, and its treatment is discussed on p 377

The Acidophil or Eosinophil Adenoma.—This gives rise to the clinical conditions of gigantism or acromegaly according to the age of the patient. In [illegible] Deep X-ray [illegible] ur [illegible] se [illegible] to [illegible] no treatment unless signs o[illegible] often the case (see p. 377). Diabetes [illegible] ntly associated with this type of tumour, and when present will require appropriate treatment (see pp. 289, 356).

The Basophil Adenoma.—The part played by basophilism in the production of Cushing's syndrome and the treatment of the condition has been discussed on p. 373.

PITUITARY DWARFISM

Pituitary dwarfism, which generally becomes manifest before the tenth year *of life, is due to a defective production of the growth hormone and is frequently*

associated with a failure of the gonadotrophic secretions. The clinical picture is one of dwarfism with defective development of the primary and secondary sex characters. The emotional state, although sometimes unaffected, generally remains childish.

At present there is no anterior pituitary growth hormone on the market which seems to be effective. An attempt should be made to stimulate the development of the sex hormone by the intramuscular injection of chorionic gonadotrophic hormone (see pp. 381, 389). This treatment should be started about the age of twelve. Interrupted courses should be given of 2,000 units twice a week for six weeks, with an interval of three months between the courses. The results are not impressive Androgen replacement is of value in older boys in whom gonadotrophin treatment has failed (see p. 378).

HYPOPITUITARISM

Hypopituitarism, characterized by considerable weakness of the muscles, premature senility and failure of thyroid, adrenal and sexual function, results from destruction of the anterior lobe of the pituitary with consequent deficiency of its hormones. The causal factor may be tumour, syphilis, tuberculosis, cystic degeneration, embolism or thrombosis Thrombosis, usually ensuing after [illegible] vosa [illegible] ular [illegible] the patient's behaviour and in certain clinical characteristics. It is important to make the distinction, since the treatment of each is quite different.

A completely satisfactory replacement of all the absent anterior pituitary hormones is at present impossible, but corticotrophin or cortisone is capable of producing remarkable clinical improvement. Theoretically corticotrophin would seem to be the ideal treatment, but in practice cortisone appears to be as effective and is much more convenient to use. For maintenance treatment only small daily doses of from 12 5 to 25 mg are necessary, and with such replacement therapy the undesirable side-effects of cortisone are not encountered. This may be the only treatment necessary and it usually transfigures the patient within a few weeks Anabolic steroids which encourage the retention of nitrogen, salt and water also produce improvement, and of these testosterone is the drug of choice. It can be administered most economically by the implantation of 400 to 600 mg, the process being repeated if necessary every five to ten months. The technique for implantation is the same as that used for DCA (see p. 373) In severe cases 25 mg of the drug can be given daily by intramuscular injection till improvement occurs, after which the interval between [illegible] 5 mg. [illegible] ild be [illegible] It is seldom wise even then to give more than 60 mg (1 gr) of thyroid or 0·1 mg of thyroxine a day, as these patients are apt to be peculiarly sensitive to the drug A high intake of protein is also very desirable, but may be difficult initially owing to the anorexia which is such a characteristic feature of the condition. The anorexia, however, improves dramatically under the influence of cortisone and testosterone so as to permit of a gradually increasing intake of protein food.

Just as patients with Addison's disease are apt to be precipitated into Addisonian crisis by any form of stress, such as an intercurrent illness or the administration of morphine or anæsthetics, so patients suffering from hypopituitarism may relapse into coma for the same reasons. Hypopituitary coma is usually [illegible]
adequat [illegible]
glycæm [illegible]
consists in the rapid intravenous administration of 250 ml. of 20 per cent. glucose solution followed by a further 500 ml. delivered by slow-drip infusion during the next twelve hours. Two hundred mg. of hydrocortisone added to the infusion are administered over the same period When hypothermia is present, every effort must be made to raise the subnormal temperature to 98° F. by hot-water bottles and by the use of a shock cage. If these measures are not rapidly successful, the patient should be immersed in a hot bath for one or two hours.

MALE HORMONE THERAPY

Much has been written about the use of the male hormone, testosterone and its esters, but it must be confessed that their value in therapeutics has not yet been clearly established.

The two functions of the testes, the production of spermatozoa and the secretion of the male hormone, are regulated by the gonadotrophic hormones secreted by the anterior lobe of the pituitary. As far as spermatogenesis is concerned, there is no method at present available for initiating or restoring the power to produce spermatozoa, and the therapeutic functions of the male hormone are limited to the remedy of any defects produced by absence or deficiency of the internal secretion of the testes. It is therefore of importance to appreciate the effects of testicular insufficiency. These vary according to whether the insufficiency commences before or after the onset of puberty. In the former case a state of eunuchoidism is produced, characterized by excessive length of the limbs, poor muscular development, high-pitched voice, female type of thyroid cartilage and lack of facial and pubic hair. When testicular insufficiency occurs after puberty there is no skeletal abnormality, but there may be excessive deposition of adipose tissue in the mammary, trochanteric and pubic regions. The skin is soft and dry with soft hair of the feminine type, the complexion is pale and there may [illegible] menopause. Sexual functions a [illegible] ierally decrease in the siz [illegible] otum. Psychological abnormalities are described, but it is uncertain whether these are due directly to lack of testicular hormone, to deterioration of the intellect resulting from premature senility or to the mental disturbance associated with the consciousness of impotence.

The chief indication for male hormone therapy is *eunuchoidism*, whether due to defective development or to castration It is well, however, to remember that many boys mature late, so that it is foolish psychologically, and may actually [illegible] since it

[illegible]

for at least six months. Oral administration is expensive and less certain in clinical effect, but methyl testosterone in doses up to 50 mg. daily by sublingual administration is [illegible] are noted withi[illegible] become larger, [illegible] those found in [illegible] often a return of sexual desire

Though testosterone therapy may bring about considerable development in the external genitalia of eunuchs and may even stimulate in them libido and potentia, it must be emphasized that it has no such effects in adult males who do not show evidence of endocrine disorder In the writer's opinion the practice of prescribing testosterone as treatment for male impotence, sterility and sometimes even as an aphrodisiac is justifiable on no sound clinical evidence nor on any theoretical consideration A great deal of male impotence is, of course, psychological in origin and the injection of male hormone may act as a psychological stimulus, in small doses it may do no harm except to the patient's pocket, but in large doses it will inhibit spermatogenesis. Recent studies in male sterility by means of testicular biopsies have divided the organic cases into two classes: the first exhibits degeneration in the seminiferous tubules with surrounding fibrosis, thought to be due to infection or to a nutritional defect; the second exhibits tubular impairment without fibrosis, which is assumed to indicate pituitary gonadotrophic deficiency. The most rational treatment for this latter class is the injection of follicle-stimulating gonadotrophic hormone (see p. 381), but unequivocal success is rare Treatment by testosterone is certainly irrational, because actual experiment has shown that it produces shrunken germinal cells in the seminiferous tubules. It is possible, however, that very small doses may stimulate the secretion of the prostate and seminal vesicles (see p. 392)

Among other indications for androgen therapy may be mentioned *Undescended Testes* and *Premature Senility*. It is extremely doubtful, however, whether any good effect can really be attributed to their treatment with androgen. The literature is not convincing, and in the present state of knowledge it seems unwise to use the androgens as a routine therapeutic measure for these conditions. Some workers have recommended the administration of testosterone to the female for the treatment of metropathia (see p. 385)

[illegible] *musculature consequent on its anabolic action on nitrogen metabolism. Thus* it may be used not only in hypopituitarism (see p 377) but to assist in the correction of other conditions associated with a severely negative nitrogen balance, particularly in the preparation of cachectic patients for surgery. The value of testosterone in the palliative treatment of metastatic cancer of the breast is discussed on p. 469.

D. M. DUNLOP.

FEMALE SEX ENDOCRINOLOGY

INTRODUCTION

The intelligent treatment of menstrual and reproductive abnormalities

ses involved in

actions of the

The following is a brief epitome of the cyclical changes which occur in the ovaries and

function are: (*a*) the follicle-stimulating hormone or FSH, (*b*) the luteinizing hormone or LH, sometimes referred to as the interstitial-cell-stimulating hormone or ICSH, (*c*) the luteotrophic hormone or prolactin.

2. The ovaries, stimulated by the follicle-stimulating hormone of the hypophysis, give rise to several Graafian follicles, which during their development elaborate œstradiol under the stimulus of the luteinizing hormone. Œstradiol is the true female sex hormone which promotes the development of the reproductive tract and secondary sex characteristics. It has a growth-stimulating effect on the uterine endometrium inducing the pre-ovulatory or proliferative phase.

3. One follicle in each ovarian cycle reaches full development and ruptures on the surface of the ovary releasing an ovum—ovulation. This phenomenon usually occurs on the 12th, 13th or 14th day of the cycle, counting the first day of menstruation as Day No. 1. The ruptured follicle, under the stimulus of the pituitary luteinizing hormone, undergoes a characteristic change; it becomes luteinized and a corpus luteum forms The corpus luteum also elaborates a specific luteal or progestational hormone—progesterone, which is activated by the pituitary luteotrophic hormone. The corpus luteum also secretes œstradiol.

uterine endometrium

al phase.

, breaks down when

l in the uterus about the 23rd or 24th day of the cycle. At the site of implantation a chorionic hormone is elaborated which maintains the activity of the corpus luteum, now termed the corpus luteum of pregnancy. The concentration of the luteal hormones increases as a result of the renewed stimulus from the chorionic hormone so that the integrity of the endometrium is maintained.

Although there are many hypotheses, menstrual bleeding can best be explained on the basis of diminishing corpus luteum activity with a consequent lowering of the concentration of the luteal hormones below a level adequate to maintain intact the endometrial structure.

It is difficult to estimate the importance of the role played by certain of the other endocrine glands, such as the thyroid, adrenals and pancreas, in menstrual and reproductive function. All are essential to a general hormonal balance, and there is evidence to suggest that dysfunction of any one of these glands may adversely affect the menstrual and reproductive process. Chief interest, however, has been centred around the glands vitally concerned in the menstrual function, namely, the pituitary and ovaries

Gonadotrophic Hormones

It has been conclusively demonstrated that anterior pituitary gland extracts are effective in stimulating gonadal function in the hypophysectomized experimental animal. Such extracts would be of very great value in the treatment of patients exhibiting ovarian hypofunction. Potent extracts, however, are not only very difficult to prepare, but they are so unstable that they readily lose their potency. At the present time there are no reliable *anterior pituitary gland* extracts available for clinical use. There are, however, two preparations which, though not truly hypophyseal in character, have an anterior pituitary-like action. From the point of view of their therapeutic application, it is most important that the biological effect of these two substances should be clearly understood.

The substances are:

1. Urine or chorionic gonadotrophic hormone.
2. Serum or equine gonadotrophic hormone.

Urine Gonadotrophic Hormone.—This hormone is present in the urine in considerable concentration during pregnancy and is the basis of the various biological tests for the detection of early pregnancy. It can be extracted from the placenta and is excreted in the urine in cases of chorion epithelioma and certain embryonic testicular tumours. Thus it is extra-hypophyseal in origin and the available evidence indicates that it is elaborated by chorionic tissue. The predominant effect of this autacoid on the ovaries of immature animals is luteinization. The administration of this hormone does *not* stimulate the development of Graafian follicles in humans, but it may produce luteinization in follicles already formed. The indications for its clinical use, therefore, are limited.

Serum Gonadotrophic Hormone.—The blood serum of pregnant mares contains a hormone the effect of which simulates rather closely the follicle-[illegible]

by the simultaneous administration of chorionic gonadotrophic hormone.

[illegible]

in terms of an international standard has clarified the previous difficulty in [illegible]

[illegible] pituitary and anterior pituitary-like preparations are not effective when given orally. These preparations should be given by the intramuscular or intravenous route. When a powder preparation is used it should be carefully dissolved in the solvent and the site of injection thoroughly massaged. This precaution avoids or minimizes any local or general reaction to the injection. Intravenous administration should be preceded by a skin sensitivity test in order to avoid unfavourable reactions. Anterior pituitary and anterior pituitary-like preparations retain their optimum potency when kept in a refrigerator.

Although there can be no doubt as to the biological effects of urine and

Several courses of this treatment may be required before the condition is brought under control. Occasionally *a period of amenorrhœa, varying in duration from* two to three months, may be produced as a result of this therapy, after which there is a return of the normal cycle. The administration of testosterone is not without risk; it is sometimes associated with disturbing reactions such as hirsutism, enlargement of the clitoris and huskiness of the voice. Fortunately these reactions are generally reversible and can be minimized by restricting the total dosage during a menstrual cycle to 0·25 g.

Surgical Treatment.—Curettage of the uterus is sometimes essential for the control of severe bleeding; it is also frequently necessary for diagnostic purposes. Curettage alone has a curative effect in many of these cases, and this being so, it is only reasonable that this simple form of therapy should be employed and its effect assessed before resorting to any more major surgical procedure. It is possible sometimes to rupture a thin-walled follicular cyst under anæsthesia or even to manipulate it into the Pouch of Douglas and aspirate it through the posterior fornix. Bilateral resection of enlarged ovaries is favoured by some authorities When all conservative forms of therapy, including curettage or repeated curettage, fail to control the bleeding, the induction of an artificial menopause is indicated, especially in women over the age of forty. This is probably best accomplished by total hysterectomy with conservation of one or both ovaries.

Irradiation.—The induction of an artificial menopause with radium or X-irradiation of the ovaries is certainly an effective therapeutic measure for menopausal patients, but has the disadvantage that it is frequently followed by severe menopausal disturbances There is also some evidence to indicate that there is a greater tendency in these case
the uterus at a later date. Radium or
reserved for patients who are poor surgic
of treatment in younger women with the object of inducing temporary amenorrhœa is fraught with considerable danger as there is a marked variation in individual sensitivity to irradiation. A dosage adequate to induce six to nine months' amenorrhœa in one patient may produce permanent ablation of ovarian function in another; its use, therefore, in such cases is not advised.

Menorrhagia.—Menorrhagia or excessive menstrual loss is most frequently due to some pathological lesion in the pelvis.
be excluded in all cases by a detailed pelv
causative factor is a systemic disturbance s
dyscrasia The causative factor in some may be an undetectable low-grade infection of the pelvic tissues, and in others over-exertion or psychological trauma. There remains a small number of patients in whom no apparent cause for the menorrhagia can be found, and in such cases it is assumed that the menorrhagia is due to a hormonal imbalance

Treatment.—The general measures advocated for metropathia hæmorrhagica are also applicable in cases of menorrhagia Short-wave diathermy is effective when the ætiological factor is a low-grade pelvic infection, and it is advisable to

cycle, counting the first day of menstruation as Day No. 1, and cont

three or four cycles, is most likely to meet with success. Curettage of the uterus frequently relieves menorrhagia, and more particularly when it is due to an endometrial defect. It should always be carried out before proceeding to major surgical procedures. When conservative measures fail to control the menorrhagia, especially in women over the age of forty, an artificial menopause should be induced. Hysterectomy may have to be considered in the exceptional case even at an earlier age

Polymenorrhœa—Polymenorrhœa or frequent menstruation generally causes no constitutional disturbance when the cycle is regular and the loss normal, and therefore requires no treatment. Excessive menstrual loss, however, must be treated, and this should be along the lines indicated for menorrhagia.

Amenorrhœa

Amenorrhœa, or cessation of menstruation, may represent a physiological process, may be an expression of a functional disturbance or a manifestation of a pathological condition.

Absence of menstruation is physiological before puberty, during pregnancy and lactation, and after the menopause

A functional disturbance is a common and frequent cause of secondary amenorrhœa The anterior pituitary gland, through its dominant control of the activity of the ovaries, regulates the menstrual process The function of the anterior pituitary, however, is governed by the hypothalamus, which is influenced in some measure by the higher cerebral centres and autonomic nervous system. Abnormal nervous stimuli arising in the higher cerebral centres are generally inhibitory to the hypothalamus and thus to pituitary activity Psychological disturbances, such as grief, worry or disappointment, especially in those susceptible to psychological trauma, distort the normal nervous control of the hypothalamus and pituitary and lead to hypophyseal hypofunction The ovaries and uterus in these cases are capable of being stimulated, it is the hormonal stimulus which is deficient or absent.

Pathological lesions of the endocrine glands, particularly the pituitary, ovaries, pancreas and adrenals, are important causes of amenorrhœa. Equally important are lesions of the reproductive tract Systemic diseases, such as [illegible]

[illegible]

[illegible] rhœa indicates that there is no specific line of treatment, and that only by a review of all the facts accruing from interrogation, examination and investigation of the patient can any rational form of therapy be suggested

In elucidating the patient's history it is important to ascertain if there has been any abnormal psychological stimulus, such as grief, worry, fear, change of surroundings or occupation, etc, within a short time prior to the onset of the amenorrhœa Pregnancy must be excluded in every case This can readily be done without the patient's knowledge, if there is any doubt, by testing a specimen of urine for chorionic gonadotrophic hormone. Tests for pregnancy are carried out at various pregnancy diagnosis laboratories, in Scotland the centre is the Pregnancy Diagnosis Laboratory, Usher Institute, Warrender Park Road, Edinburgh Six fluid ounces of the urine first voided in the morning, without the addition of preservative, should be despatched The Hogben or toad test gives a result in twenty-four hours at a cost of ten shillings.

Several courses of this treatment may be required before the condition is brought under control Occasionally a period of amenorrhœa, varying in duration from two to three months, may be produced as a result of this therapy, after which there is a return of the normal cycle. The administration of testosterone is not without risk, it is sometimes associated with disturbing reactions such as hirsutism, enlargement of the clitoris and huskiness of the voice. Fortunately these reactions are generally reversible and can be minimized by restricting the total dosage during a menstrual cycle to 0 25 g.

Surgical Treatment.—Curettage of the uterus is sometimes essential for the control of severe bleeding, it is also frequently necessary for diagnostic purposes. Curettage alone has a curative effect in many of these cases, and this being so, it is only reasonable that this simple form of therapy should be employed and its effect assessed before resorting to any more major surgical procedure. It is possible sometimes to rupture a thin-walled follicular cyst under anæsthesia or even to manipulate it into the Pouch of Douglas and aspirate it through the posterior fornix. Bilateral resection of enlarged ovaries *is favoured by some authorities. When all conservative forms of therapy, including curettage or repeated curettage, fail to control the bleeding, the* induction of an artificial menopause is indicated, especially in women over the age of forty. This is probably best accomplished by total hysterectomy with conservation of one or both ovaries

Irradiation.—The induction of an artificial menopause with radium or X-irradiation of the ovaries is certainly an effective therapeutic measure for menopausal patients, but has the disadvantage that it is frequently followed by severe menopausal disturbances. There is also some evidence to indicate that there is a greater tendency in these cases for the development of malignancy in the uterus at a later date. Radium or X-irradiation therapy is probably best reserved for patients who are poor surgical risks The employment of this form of treatment in younger women with the object of inducing temporary amenorrhœa is fraught with considerable danger as there is a marked variation in individual sensitivity to irradiation A dosage adequate to induce six to nine months' amenorrhœa in one patient may produce permanent ablation of ovarian ... such cases is not advised

causative factor is a systemic disturbance s...
dyscrasia. The causative factor in some may be an undetectable low-grade infection of the pelvic tissues, and in others over-exertion or psychological trauma. *There remains a small number of patients in whom no apparent cause* for the menorrhagia can be found, and in such cases it is assumed that the menorrhagia is due to a hormonal imbalance.

Treatment.—The general measures advocated for metropathia hæmorrhagica ... Short-wave diathermy is effective ... visable to ... py is not ... lways be ... thyl ... the ... over

cycle, counting the first day of menstruation as Day No. 1, and ...

treatment, occurs from a secretory endometrium and is indistinguishable from a normal period. It is advisable during the subsequent three months to give ethinyl œstradiol, 0·05 mg. daily, along with ethisterone, 10 mg. thrice daily, from the fifteenth to the twenty-fourth day of each cycle.

Some authorities favour the use of gonadotrophic hormones. Theoretically this is the ideal method of treatment, as in the majority of cases of amenorrhœa it is the pituitary stimulus to the ovaries which is deficient or absent. The following scheme of treatment is suggested: Serum gonadotrophic hormone, 1,000 I.U., combined with urine gonadotrophic hormone, 500 I.U., is given every third day until five injections have been given. After an interval of ten to fourteen days the same course is repeated. It may be necessary to give several courses of these preparations before any effect is produced, and it is advisable to continue their administration during the first half of the cycle for a period of three months after menstruation has been established. The results obtained with gonadotrophins have been disappointing. It may be that in the past the dosage of hormone employed has been too low and that better results would be obtained were the dosage markedly increased.

Minor Menstrual Disorders

Hypomenorrhœa.—Scanty menstrual loss is frequently associated with a normal ovarian and uterine cycle and generally requires no treatment. In such cases conception is possible. In some women, however, a scanty loss is associated with failure of ovulation so that there is an incomplete ovarian and uterine cycle. This type of menstruation is termed *anovular* and is a causative factor in sterility. It can be detected either by the histological examination of the endometrium removed immediately prior to the onset of menstruation, when a pre-ovulatory or proliferative endometrium is found instead of the normal secretory phase, or by the failure to detect pregnanediol in the urine examined during the second half of the menstrual cycle. Further, this type of menstruation should be suspected when the basal temperature remains monophasic throughout the menstrual cycle. There is no preparation available at present which will induce ovulation.

Oligomenorrhœa.—This is the term applied to menstruation which is delayed regularly one, two or three weeks. The condition is common and may occur in conjunction with a complete or incomplete ovarian cycle. It is important in that it is frequently associated with lassitude and a feeling of depression and irritability during the time menstruation is delayed and may also be a precursor of amenorrhœa. The condition is due to a delayed or defective pituitary stimulus and theoretically should best be treated by supplementary gonadotrophic hormone therapy, but the best results are obtained with cyclical œstrogen and progesterone therapy as advised in the treatment of amenorrhœa.

Mid-Menstrual or Ovular Bleeding.—This is not uncommon. The bleeding is usually very scanty, but may be as much as a normal period. It occurs at the time of ovulation and it is believed to be associated with either an endometrial defect or a temporary diminution in the blood concentration of œstrogen just before this is made good by the developing corpus luteum. It is

Systemic disease must be excluded by a detailed physical examination supplemented if necessary by the investigative facilities available in a well-equipped laboratory. The exclusion of pathological lesions may involve considerable investigation such as pelvic examination under anæsthesia and curettage of the uterus, urinary hormone analysis, radiological examination of the chest and the sella turcica, etc *When a definite lesion* can be demonstrated as the cause of the amenorrhœa, then the treatment is that of the lesion. When no cause can be found, then the amenorrhœa may be considered functional in origin.

When there is a history of a psychological disturbance, it is important to explain in simple language to the patient and to her relatives the cause of the amenorrhœa. Furthermore, it is advisable to reassure the patient that the cessation of the menses *per se* does not interfere with general health ; nor does it [illegible]

It is always advisable, however, to indicate to the prospective husband that although the amenorrhœa does not interfere with sexual life, the likelihood of [illegible]

spontaneously after a period of one year, it is not advisable to delay the institution of treatment any longer than this, and not so long if reassurance does not allay the anxiety.

Before considering hormone therapy it is advisable to concentrate on improving the general health of the patient. Occupations involving considerable strain and worry should be avoided Adequate rest and exercise in the open air should be advised. Iron therapy is frequently indicated. As there is a tendency to obesity in many of these patients, a suitable anti-obesity régime should be instituted if required (see p 324). Conversely, if the patient is markedly under weight, every effort should be made to improve nutrition.

When the amenorrhœa persists after the general health and nutrition have been improved, *hormone therapy is often valuable. There is always a tendency,* after a prolonged period of amenorrhœa, for the uterus to undergo a certain degree of hypoplasia, and it is probably advisable initially to promote full uterine development. With this aim in view ethinyl œstradiol, 0 05 mg. (or stilbœstrol, 5 mg.), should be given daily for a period of twenty-four days. If uterine bleeding does not occur within seven days of cessation of treatment, another course of œstrogen similar to the first should be given, and in some cases a third course may have to be given if no bleeding supervenes within seven days after treatment. The induction of uterine bleeding may be taken as a rough index of full uterine development Although the bleeding is not normal menstrual loss, but is due rather to withdrawal of the œstrogen, it may have a beneficial psychological effect on a susceptible subject, especially when the amenorrhœa is of short duration. Failure to induce bleeding with repeated courses of œstrogen therapy indicates that the uterine endometrium is refractory to hormonal stimulus and that little can be done to re-establish the menstrual cycle. Such cases are rare. When bleeding has been induced, a further twenty-four-day course of œstrogen should be given, starting on the first day of the bleeding and

production of œstrogen. The administration of œstrogen during the second half of the menstrual cycles corrects this imbalance. As it is impossible by present-day methods to estimate the degree of the œstrogen-progesterone imbalance, the effective dosage of œstrogen can only be obtained by trial and error. The following scheme is recommended:

During the first cycle 0·05 mg. ethinyl œstradiol is given daily from the fifteenth to the twenty-fourth day of the cycle (i.e. for ten days), counting the first day of menstruation as Day No. 1. If the next period is free from pain, this dosage is given at the same time-interval during the three following cycles. When no relief is obtained with 0·05 mg. daily, the same dosage is given twice daily during the next cycle, and if that dosage is not effective, three times the amount is given in the following cycle When the effective dose is obtained, it is continued over three or four cycles The results obtained with this form of therapy are encouraging

Surgical Treatment.—When these measures fail to relieve the dysmenorrhœa, it is important to carry out a detailed pelvic examination, preferably under anæsthesia in young girls, in order that pathological lesions in the uterus and adnex [illegible]
patho [illegible]
dilate [illegible]
lines of treatment already recommended should be referred to a specialist, who may consider the injection of alcohol into the cervical ganglia of the uterus, paravertebral block or the division of the presacral nerve

STERILITY

Sterility may be defined as failure to conceive after a period of three years of normal married life This interval of time is, however, arbitrary, a barren couple over the age of thirty may require investigation after a much shorter interval.

[illegible]

dista, excessive coitus, dyspareunia and vaginismus may have an unfavourable effect on conception A pelvic examination is necessary in order to exclude gross lesions of the reproductive tract The exclusion of systemic disease such as active pulmonary tuberculosis, severe cardiac disease and chronic kidney lesions is of paramount importance in regard to childbearing. It requires delicate judgment to decide whether pregnancy is desirable or even advisable in [illegible]

investigation is carried out. Examination includes a history of previous illnesses and infections, general examination, examination of the genitalia and of the seminal fluid The instructions which should be given to the husband regarding the collection of seminal fluid are as follows

(1) Three or four days' continence should be observed.

(2) The seminal fluid, obtained either by manipulation or coitus interruptus, should be collected in a small wide-mouthed glass jar which has been very thoroughly washed The condom or rubber sheath is not suitable for the collec-

of no serious significance in the unmarried woman except for its inconvenience, but it may be a cause of sterility in the married woman.

The daily injection of 5 mg. progesterone, or 30 mg. ethisterone orally, for three days at the mid-menstrual interval, given over a period of three months may control the bleeding effectively.

Dysmenorrhœa

The innumerable therapeutic measures advocated for the relief of primary dysmenorrhœa indicate that many ætiological factors have to be considered and that several lines of treatment may have to be adopted before success is obtained. Thus it is evident that there is no single form of therapy suitable for every case A routine scheme of treatment is recommended, such as the following:

General Measures.—So many girls are ignorant of the elementary principles of menstrual function and sex hygiene that the first step is to allay any anxiety they may have concerning the menstrual process, and at the same time to offer guidance on the fundamentals of general health. It will be found that a brief explanation to the patient of the essentially physiological nature of the menstrual process is often helpful; doubts and superstitions gathered from misguided parents or ill-informed companions can often be dispelled. Every

games, to have the daily bath and to pursue their everyday activities. As constipation is a common ætiological factor, particularly when present during the pre-menstrual phase, a regular evacuation of the bowels should be ensured by instituting the measures recommended on p. 499. The adoption of these general measures alone often results in alleviation of the menstrual pain.

Sedative Treatment.—Mild analgesics, such as aspirin, 0 3 g. (5 gr.) three times a day, reinforced where necessary by codeine, 15 mg ($\frac{1}{4}$ gr.), and phenacetin, 0·3 g. (5 gr.), when the pain is severe, are often efficacious In view of the danger of habit formation it is undesirable to prescribe opiates or pethidine, or to acquiesce in the use of any form of alcohol.

Hormone Therapy.—Menstruation can always be rendered painless by

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5 mg.)

twice daily, from the first day of the cycle and continued for twenty days, is effective. This form of therapy, which is temporary and operates only in the cycle during which it is given, may be justifiable, on occasion, in order to tide a patient over a particular crisis, but it is not advocated as a routine treatment for all cases of dysmenorrhœa.

As dysmenorrhœa occurs in ovulatory and not in anovulatory cycles, it must be the interaction of the corpus luteum which determines whether menstruation will be painful or free from pain. The majority of young women, however, have ovulatory cycles and no dysmenorrhœa, indicating that the luteal hormones —œstrogen and progesterone—act synergistically. We believe that the dominant factor in painful menstruation is an œstrogen-progesterone imbalance and that the imbalance is due to an excessive secretion of progesterone or diminished

temperature over several months the approximate time of ovulation can be detected. This applies to an irregular as well as to a regular cycle. A good working rule which applies to all cases is to advise the couple to restrict coitus for the first month to the week immediately after the period; for the second month to the second week after the period, and for the third month to the third week after the period. It is hoped thereby that coitus and ovulation may coincide.

Although the physiology of the spermatozoa is not yet fully understood, it is known that the addition of Ringer's glucose to the seminal pool reactivates many sluggish spermatozoa and may induce the necessary vigour for their gyrations [illegible] aginal douche with [illegible] 1 chloride 0·23 g, [illegible] to 1,000 ml) may [illegible] essaries containing fructose are now available and are more convenient than the pre-coital douche.

Failure to conceive after six months of this régime indicates that further investigation is necessary, and the patient should be referred to a specialist. The patency of the Fallopian tubes will have to be investigated, and this can be [illegible] of pregnanediol excretion in the urine or by endometrial biopsy. The reaction of the vaginal secretions, seminal fluid and seminal pool require investigation as well as the seminal permeation of the cervical mucus. Dilatation of the cervix alone is frequently a successful therapeutic measure. Artificial insemination may have to be considered in some cases where a structural genital defect in the male precludes normal intromission.

RECURRENT ABORTION

Ten per cent. of all pregnancies end in spontaneous abortion. An incidental [illegible] one abortion is 86 per cent. and after two abortions 63 per cent. A patient, therefore, who has had two consecutive abortions has two chances out of three of continuing a third pregnancy to term without treatment. When three consecutive abortions have occurred, however, the spontaneous cure rate in the fourth pregnancy falls to 16 per cent., or, in other words, a patient who has had three consecutive abortions has only one chance in six of continuing a fourth gestation to term without treatment. There is such a marked difference in the spontaneous cure rate between two and three miscarriages that the term "recurrent" refers exclusively to three or more spontaneous abortions.

Management.—It is important in the management of a patient who aborts repeatedly that she should have a thorough physical examination prior to the next conception, and any systemic disease treated. Lesions of the reproductive tract such as retroversion of the uterus and cervical lacerations must be corrected. The blood should be tested for the Wassermann reaction, and if positive, specific therapy should be instituted. It is now recognized, however, that syphilis is not a common cause of recurrent abortion, especially in the early months. Although so far there is no clear evidence that blood incompatibility

tion of specimens as the impurities in the rubber and the powder necessary for
the use

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compete

The total volume of the ejaculate of a normal fertile male should be 4·5 ml. with a spermatozoa count of 100,000,000 per ml. A count below 60,000,000 is generally considered unsatisfactory, but conception has been known to occur with counts as low as 10,000,000. Twenty per cent. of abnormal forms is within the range of normality. The ejaculate must be free from blood and pus. The spermatozoa should retain some motility for a period of four hours after ejaculation.

Azoospermia or complete absence of spermatozoa in the ejaculate suggests that there is absolute sterility, but several specimens should be examined before this assumption is confirmed. The patient, however, should be referred to a urologist for testicular biopsy in order to determine whether the azoöspermia is due to defective spermatogenesis resulting from atrophy of the seminiferous tubules or to a blockage in the seminal tract. At present there is no effective treatment for the former; occasionally operative treatment is successful for the latter.

Oligospermia or sub-normal spermatogenesis is common, but as many extrinsic factors influence spermatogenesis, a definite diagnosis should be made

500 I.U., should be given every second day over a period of one month; the course may be repeated after an interval of two or three weeks. Testosterone propionate in large doses depresses spermatogenesis, but small doses of the order of 5 mg. twice weekly may possibly be beneficial. The androgenic hormone does not influence spermatogenesis but stimulates the secretion of the prostate and seminal vesicles and thus creates a more normal seminal pool. This therapy should therefore be given in conjunction with the anterior-pituitary-like preparations.

When the male has been found to be potent and no gross abnormality can be detected in the female, then the management suggested is as follows:

The couple should be instructed to make every effort to become as physically fit as possible. They should have sufficient exercise, adequate sleep, and a full diet especially rich in protein. Alcohol and drugs, if not interdicted, must at least be restricted

They should be advised regarding the optimum time for conception. It is now recognized that ovulation occurs, in the majority of women with a normal twenty-eight day cycle, about fourteen days prior to the menstrual period. It therefore follows that coitus about the twelfth to fourteenth day of the cycle, counting the first day of menstruation as Day No. 1, gives the best chance for conception. This rule does not obtain for all women, and especially those with an abnormal cycle Information regarding the time of ovulation can be obtained by recording the basal temperature daily. The rectal temperature, when recorded immediately before rising each morning, is shown to fall at ovulation. This is followed by a rise of a few fractions of a degree and it continues at this slightly higher level until the onset of menstruation. By charting the daily

need rarely be employed. When breast feeding is clearly contra-indicated, œstrogen therapy should be started on the day after delivery, in which case milk rarely appears in the breasts

(Estrogens are also of value in reducing milk secretion during the weaning [illegible]

THE MENOPAUSE

[illegible]

of discomfort experienced, apart from any menstrual disturbance, depends in large measure on the woman's temperament and outlook Some women, especially those with large families who are haunted by the fear and anxiety of further child-bearing or those who suffer from intense menstrual discomfort, welcome the relief which the menopause brings Generally such women have little trouble or discomfort Others, however, who have longed for marriage or motherhood realize the significance of the advancing years and view the climac- [illegible]

age", which have been, and unfortunately still are, employed to describe this phase, suggests to them something mysterious and foreboding These women may experience considerable distress and discomfort

General Management.—A simple explanation of the significance of the menopause is reassuring and of considerable benefit, particularly as many women reach the menopause without any clear understanding of what it means Their knowledge, as a general rule, is based on misinformed conversation or [illegible]

women at the climacteric tend to relax, overeat and lose interest in their appearance They should be advised that sexual desire does not diminish when menstruation ceases, but sometimes increases and may continue for many years Minor menopausal symptoms such as the infrequent hot flush, irritability and depression usually respond to simple measures. Reassurance and the administration of a mild sedative such as phenobarbitone, 30 mg (½ gr) once or twice daily for a few weeks, are usually beneficial

The occurrence of prolonged and excessive bleeding at the menopause should be an indication for immediate investigation. Malignancy of the reproductive tract must be excluded by a detailed pelvic examination and curettage of the uterus. Curettage may prove to be curative as well as diagnostic, but in a proportion of cases the excessive loss will continue and the induction of an artificial menopause will become necessary

Severe menopausal symptoms, such as frequent hot flushes, intense head-

is an exciting factor in habitual abortion, it may be advisable to investigate the rhesus grouping of both partners (see p. 862). The patient should be given definite instructions to be followed when conception occurs. She should be

four months of pregnancy. The importance of rest must be emphasized, and complete rest in bed is desirable during the time when the periods would occur had not pregnancy intervened Attention should be directed to the careful regulation of the bowel in order to avoid the necessity for drastic purgation, which might be disastrous. She should be told that any suspicion of vaginal bleeding is an indication for the immediate cessation of all activities. The importance of constant encouragement and reassurance cannot be over-emphasized.

Specific Therapy.—The administration intramuscularly of 20 mg. progesterone twice weekly or 30 mg. ethisterone by mouth daily, during the first four months of pregnancy, is frequently successful. The same dose should be given thrice daily if bleeding occurs and should be continued until it ceases. There is evidence that in some cases of recurrent abortion the progestational hormone may not be deficient but imperfectly metabolized. The imperfect

LACTATIONAL DISORDERS

Stimulation of Lactation.—The success of breast feeding depends in large measure on the adequate preparation of the breasts during pregnancy

difficulty in

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ricated with

When the

supply of milk is inadequate to meet the demands of the infant, an increase in the fluid intake in the form of extra milk, water and nutrient drinks such as Lactagol, Milo, etc , should be advised. Hot and cold plotting of the breasts is sometimes beneficial. Complete emptying of the breasts after each feed stimulates an increased secretion When these measures fail, supplementary feeding becomes necessary, at least as a temporary measure

Inhibition of Lactation.—The marked engorgement of the breasts which sometimes occurs about the fourth or fifth day of the puerperium can cause acute discomfort. It is readily relieved by the administration of 10 mg. stilbœstrol, which may occasionally have to be repeated. The inhibition of lactation can readily be accomplished, without the discomfort of tight binding of the breasts

which has an

the anterior p

daily for four

in almost all cases Synthetic œstrogens, as a general rule, are well tolerated during pregnancy and the puerperium, and therefore the natural œstrogens

Post-Menopausal Disturbances

Several conditions may develop at varying intervals after the menopause which may be directly or indirectly associated with the cessation of ovarian activity.

Senile Vaginitis.—This is an inflammatory condition of the vaginal mucosa which is due primarily to an œstrogen deficiency. The vaginal walls, which are [illegible]

[illegible]

inguity for a period of two or three weeks.

Kraurosis Vulvæ.—The condition is characterized by shrinkage and atrophy of the vulvar tissues, which in the early stages have a reddish appearance but later assume a distinctive yellow coloration. The irritation, dysuria, dyspareunia and vulvar ache are often relieved by œstrogen therapy given along the lines advocated for senile vaginitis. The application of sedative lotions or 5 per cent. cocaine ointment is sometimes of value when the œstrogens fail. A plastic vulvar operation is sometimes necessary for the relief of dyspareunia.

Leucoplakia Vulvæ.—This condition is important in that it strongly predisposes to carcinoma of the vulva. In the early stages the vulva is red, but later it assumes a distinctiv[illegible] fissures are prone to occur [illegible] is sometimes rel[illegible]

[illegible]

become swollen and painful. The arthritis is possibly due to vascular changes in the joints subsequent to cessation of ovarian function. In the early stages œstrogen in the form of ethinyl œstradiol, 0.05 mg. twice daily in twenty-day courses, with an interval of two weeks between each course, may prove beneficial and should be employed as an adjuvant to other forms of treatment.

Menopausal Psychosis.—Mild depression is a common feature of the menopausal syndrome and in the majority of cases responds satisfactorily to simple measures. There are, however, some cases, especially those with an unsound hereditary background, which react unfavourably to the menopausal disturbances and become definitely psychotic. Much can be done by encouragement, sedatives and œstrogen therapy to tide these patients over this crisis, but institutional treatment is sometimes necessary. The duration of stay in hospital may be appreciably shortened by a continuation of œstrogen therapy.

T. N. MACGREGOR.

[APPENDIX

ache, vertigo, insomnia, palpitation, dyspnœa and emotional instability, mimic those of any systemic disease. As organic lesions related to the head, blood vessels, kidneys and pelvic organs are prone to become manifest during this phase of life, it is important that organic disease should be excluded before [illegible] the difficulty, although it may be time-consuming; and she should receive encouragement and assistance while she is making the readjustment.

Specific Treatment.—The œstrogens are of great value in the alleviation of severe menopausal symptoms. Prompt control of symptoms by the administration of adequate amounts of œstrogen has a beneficial psychological effect, and as a rule changes the patient's whole outlook. She rapidly regains a feeling of well-being, is able to concentrate, enjoys undisturbed sleep and can carry out her daily routine. Œstrogen in adequate dosage restores in some measure the hormonal balance, and subsequently gradual withdrawal of the dose permits the endocrine system to adjust itself to the absence of the ovarian secretions.

The synthetic œstrogens given orally are generally most effective. The [illegible] thrice daily until all the symptoms are controlled; this usually occurs in three to five days. Thereafter the same dosage of ethinyl œstradiol is given daily for one week and every second day for a further week. The interval between each dose is then increased so that by the end of two months only one tablet is being taken weekly. Generally no further treatment is required, but on occasion the course may have to be repeated. When the synthetic œstrogens are not well [illegible] over the ensuing seven to eight weeks.

Some women develop vasomotor and nervous symptoms years after the menopause. They react favourably to the scheme of œstrogenic therapy outlined above, but a maintenance dose of the hormone may have to be given over a prolonged period

The administration of œstrogen, especially if it is prolonged, reactivates the uterine endometrium in a proportion of cases and bleeding occurs when the œstrogen is reduced or withdrawn Every patient having œstrogen therapy should be warned that such a complication may arise, otherwise it may cause [illegible] menopause. The [illegible] It is therefore advisable to stop all treatment if bleeding supervenes and keep the patient under review. If the bleeding recurs, malignancy must be excluded without delay by a detailed investigation of the reproductive tract, including curettage of the uterus.

DISORDERS OF THE BLOOD

INTRODUCTION

I[illegible] to rely solely on the symptoms complained of or on the appearance of the patient. The symptoms of all types of anæmia are dependent mainly on anoxæmia, and their severity varies according to the degree of anoxæmia and the rapidity with which it is produced. Similarly, no sign by itself can be held to be diagnostic, and it is unwise to rely solely on the appearance of the skin, especially of exposed surfaces, for diagnosis of the type or degree of the anæmia present. Hence no short cut to correct diagnosis exists, and a careful blood examination should always be performed when anæmia is suspected. In certain types of anæmia, in which the diagnosis is obscure, examination of the peripheral blood must be supplemented by examination of the bone marrow [illegible] diagnostic features in the blood picture may be altered to such a degree that the pathologist may have great difficulty in reaching a correct diagnosis. This is particularly likely to occur if the practitioner uses a shot-gun prescription containing iron, liver extract, cyanocobalamin or folic acid, in which case it may be difficult or impossible to decide which type of therapy should be continued.

That general practitioners still rely largely on a physical examination for the diagnosis of the type of blood disease present, and not on a blood examination, is fully recognized by medical men with special experience in hæmatology. [illegible] cases of pernicious anæmia entering hospital have been diagnosed incorrectly as hypochromic anæmia and have been treated with iron for months.

Lastly, we wish to stress the need for a thorough investigation into the underlying causal factors. The value of making such investigations is twofold: first, if the causal condition is not removed, treatment of the anæmia may fail even if the appropriate hæmatinic is given; second, pathological conditions causing the anæmia may advance to an incurable stage if symptomatic treatment for the anæmia alone is prescribed. This is particularly true of malignant disease of the gastro-intestinal tract, where a considerable temporary improvement in the blood picture may result from the administration of iron, despite the progress of the cancer.

So far we have made a plea for blood examination in every case in which

APPENDIX

GONADOTROPHIC HORMONES

Anterior Pituitary Hormone

Ambinon (Organon) This preparation also contains the thyrotrophic factor
Gonadotraphon (Paines & Byrne)
Prelabon (Bayer)

Antostab (Boots)
Gestyl (Organon)

ŒSTROGENIC HORMONES

Natural Œstrogens

Benztrone (Paines & Byrne)
Dimenformon (Organon)
Gynœstrol (Roussel)
Œstradiol Benzoate (Burroughs Wellcome)

Schering)
Theelin (Parke, Davis)
Unden (Bayer)

non, Oxo)
Menopax (Clinical Products)+Calcium Lactate
Ovendosyn (Menley & James).
Pabestrol and Pabestrol D (Paines & Byrne)
Stilbœstrol (Allen & Hanburys, Bayer, Boots, Burroughs Wellcome, Organon, Oxo)
Stilbœstrol Dipropionate (Bayer, Burroughs Wellcome, Glaxo, Organon).
Syntestrin (Richter)
Synthovo (Boots).

PROGESTERONE (B P)

Intramuscular Administration

Gestone (Paines & Byrne)
Lipo-Lutin (Parke, Davis).
Luteostab (Boots).
Lutocyclin (Ciba)
Lutogyl (Roussel)
Lutren (Bayer)
Progesterone (Burroughs Wellcome, Oxo)
Progestin (British Drug Houses, Organon)

(*b*) The antimegaloblastic anæmia factors, vitamin B_{12} and folic acid.

1. Addisonian pernicious anæmia.
2. Megaloblastic (pernicious) anæmia of pregnancy.
3. Megaloblastic anæmia of infancy.
4. Megaloblastic anæmia complicating pathological conditions of the gastro-intestinal tract, e g intestinal anastomoses, tropical sprue, idiopathic steatorrhœa, etc.
5. [illegible]
6. [illegible]
7. [illegible]

(*c*) Vitamin C

Scurvy (dealt with in the section devoted to Nutritional Disorders, p 343)

(*d*) Thyroxine.

The anæmia of myxœdema (dealt with in the section devoted to the Endocrine Glands, p. 354).

II. Anæmias Due to Excessive Blood Destruction (Hæmolytic Anæmias)

(*a*) Due to congenital abnormalities of the erythrocyte.
(*b*) Due to infective, toxic or allergic factors.
(*c*) Due to hæmolysins.

III Anæmias Due to Aplasia or Hypoplasia of the Bone Marrow

Aplastic and hypoplastic anæmia.

1. Idiopathic
2. Secondary

B. MISCELLANEOUS DISORDERS OF THE BLOOD

I The Syndrome of Portal Hypertension (Splenic anæmia, Banti's disease)

II Polycythæmia

(*a*) Relative polycythæmia
(*b*) Secondary polycythæmia (erythrocytosis)
(*c*) Polycythæmia vera (erythræmia)

III Hæmorrhagic Diseases

(*a*) Due to defects in the clotting mechanism, e g. hæmophilia, Christmas disease, hypoprothrombinæmia, fibrinopenia.
(*b*) The purpuras.
1 Due to defects in, or damage to, the capillaries
2 Due to defective production, or excessive destruction of platelets.

IV Agranulocytosis

V. The Leukæmias

VI. Infectious Mononucleosis (dealt with in the section on Infectious Diseases, see p. 23)

the doctor suspects the presence of anæmia from the symptoms and physical signs, but certain clinical features in the absence of anæmia call equally for blood investigations. In chronic leukæmias, hæmolytic anæmias, hæmorrhagic diseases and agranulocytic angina, anæmia may be absent or mild in degree at certain periods. Accordingly, enlargement of the spleen, liver or lymph nodes, and unexplained hæmorrhage, sepsis, purpura or icterus, indicate the need for a blood examination which should include a red- and white-cell count, hæmoglobin estimation and examination of a stained blood film, and in some cases a differential white-cell count, platelet count, reticulocyte count, sternal puncture and other special investigations In addition, a search for, and the removal of, the causal conditions leading to anæmia as outlined below should be instituted.

There are certain forms of treatment of particular value for, and commonly employed in, widely differing types of anæmia. In order to save needless repetition regarding technique and dosage, we have dealt with such procedures in detail in certain sections, and merely refer the reader to the appropriate pages where they are advised in other forms of anæmia. A full description of iron therapy and the general measures required for the care of a case of anæmia will be found in the section on Chronic Nutritional Hypochromic Anæmia; the indicati

Anæmia ;

the heading

CLASSIFICATION

Treatment can be placed on a more rational basis if the practitioner has some simple but clear conception of the classification of diseases of the blood. The classification submitted below places the various blood disorders into two main groups . (A) the anæmias, and (B) a miscellaneous group of diseases some of which are not necessarily accompanied by anæmia but which are generally dealt with in textbooks of hæmatology

Group A is divided into three subdivisions. The obvious advantage of this classification is that cases in Group A (I) are treated by appropriate substitution therapy, namely, iron, thyroxine, cyanocobalamin, folic acid and vitamin C ; cases in Group A (II) by removal of the hæmolytic agent, where possible, or by splenectomy ; and cases in Group A (III) by removal of the causal agent, where possible, and by blood transfusion. In Group B the treatment varies in each individual disease.

A. THE ANÆMIAS

I. Anæmias Due to Deficiency of Factors Essential for Normal Blood Formation

(*a*) Iron

1. Chronic nutritional hypochromic anæmia, including the Plummer-Vinson syndrome, chlorosis, and the hypochromic anæmia of pregnancy.
2. Hypochromic anæmia of infancy and childhood
3. Post-hæmorrhagic anæmia, acute and chronic.

and severity of this form of anæmia have decreased since the years when these surveys were made. The diets taken by women of the working classes are now less unsatisfactory and living conditions have improved. Moreover, there is little doubt that more practitioners nowadays are aware of the prevalence of iron deficiency in women and can treat it satisfactorily. Accordingly the chart given on p. 402, which represents the findings of the Aberdeen survey in 1935, cannot be regarded as giving an accurate picture of the incidence and severity

[illegible]

form of iron deficiency, which was common and severe in adolescent girls, has for many years been relatively infrequent and mild in degree, due to improvement in diet and in working conditions. When a woman becomes pregnant, anæmia may develop or become accentuated because of reduced intake and assimilation of iron from alteration of appetite and diminished gastric secretion of hydrochloric acid and also because of the fœtal demands for iron. In many cases of hypochromic anæmia of pregnancy, however, hydræmia accentuates an anæmia which existed before the pregnancy began. Since the same measures for the prevention and treatment of these forms of anæmia are indicated, it is unnecessary to deal with them separately.

Prophylaxis

The three most important factors to be considered in prophylaxis are:

(*a*) **Diet.**—The most important step is improvement of the diets of women of the working classes. Already a considerable change for the better has occurred because of improvement in financial state and a greater awareness of the value of a mixed diet, but it is still important that the family doctor should know which foods are the most important sources of dietary iron (liver, flesh food, eggs, bread made from high extraction of flour, oatmeal, peas, beans and green vegetables) and that when these foodstuffs are taken in reasonable amounts deficiency of animal protein, phosphorus, vitamins and in particular of ascorbic acid is corrected simultaneously.

(*b*) **Pregnancy.**—The development of some degree of iron deficiency anæmia during pregnancy in women of the working classes is so frequent that many obstetricians believe that iron should be prescribed as a routine prophylactic measure. We accept this view and accordingly recommend that at the third or fourth month of pregnancy curative doses of iron as indicated below should be given for a month, followed by a maintenance dose (one-third of the curative dose) for the duration of pregnancy and one month afterwards. If iron is not given to all women during pregnancy, it is important that hæmoglobin

[illegible]

potentially dangerous situation encountered when the hæmoglobin level is 30 per cent. or less. Moreover, should a severe post-partum hæmorrhage occur, the patient may be able to withstand it without being precipitated into a dangerous degree of shock.

(*c*) **Menorrhagia.**—The third factor to be considered in relation to prophylaxis is menstruation. In women whose diet has been corrected as far as possible in keeping with their economic circumstances, and in whom anæmia develops

VII. Diseases of the Reticulo-endothelial System
- (*a*) Reticuloses, including Hodgkin's disease, reticulum cell sarcoma, lymphosarcoma and multiple myeloma.
- (*b*) Diseases of lipoid metabolism.
  - (1) Gaucher's disease.
  - (2) Niemann-Picks disease.
  - (3) Hand-Schuller-Christian disease.

THE ANÆMIAS DUE TO IRON DEFICIENCY

CHRONIC NUTRITIONAL HYPOCHROMIC ANÆMIA

(*Hypochromic Anæmia. Chronic Microcytic Anæmia Simple Achlorhydric Anæmia*)

Chronic nutritional hypochromic anæmia is the name given by us to the iron deficiency anæmia occurring among women of the child-bearing age who belong mainly to the poor classes of the community. The fundamental factor in its causation is the ingestion of a diet the iron content of which is insufficient to meet the demands of menstruation and pregnancy. Our investigations in Aberdeen in 1935 and in Edinburgh in 1943 indicated that a subnormal hæmoglobin level was present in some degree in 50 per cent. of working-class women and that 15 per cent. were severely anæmic. For several reasons the incidence

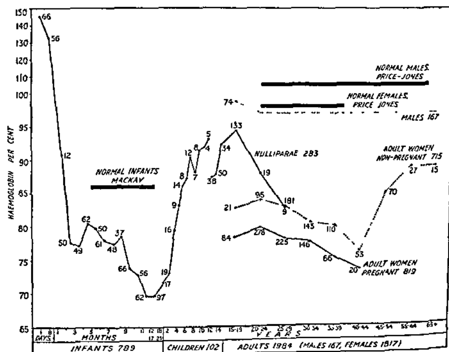


Fig. 1

Chart showing average hæmoglobin level among poor persons of all ages and both sexes

(*By courtesy of the "British Medical Journal"*)

Oral Iron Therapy.—Provided that inhibitory factors such as sepsis, toxæmia

hæmoglobin formation at that rate:

(i) iron and ammonium citrate, 2·0 g. (30 gr.) three times a day in a fluid mixture.
(ii) ferrous sulphate, 0·2 g. (3 gr.) in tablets three times a day after food.
(iii) ferrous gluconate, 0·3 g. (5 gr.), and ferrous succinate, 0·15 g. (2½ gr.) in tablets three times a day after food.

Since the above preparations in the doses mentioned are of equal potency, it would seem not unreasonable to base one's selection on their convenience, palatability and cost. Tablets are more convenient than fluid preparations because they are easily carried and do not blacken the teeth and tongue. In addition, a small bottle containing 100 tablets will last a month, whereas equivalent treatment with iron and ammonium citrate in the form of a mixture would

able. Cure of the anæmia with any of these products may be achieved at the cost of a few shillings.

When the preparation of iron to be administered has been selected it is inadvisable to start treatment with the full curative dose, since in some patients this may result in dyspepsia, vomiting or diarrhœa. Accordingly, one-third or one-half of the curative dose should be given for the first two or three days, then, if no gastro-intestinal symptoms have resulted, full dosage should be given. The development of untoward symptoms should lead to a slower increase in the dose. Ferrous gluconate and ferrous succinate are less liable to produce gastro-intestinal upset than ferrous sulphate and iron and ammonium citrate, but it is a wise plan even with these preparations to increase the dosage gradually in the way described. It is important to realize that dyspepsia may be a symptom of the anæmia itself, in which case it will be relieved only by the continuation of the iron therapy.

Lastly, iron should always be taken after meals and followed by a drink of water, as by this means the irritating effects of the mineral on the gastric mucosa are reduced to a minimum.

Duration of Iron Therapy.—The period which will elapse before a normal blood count is attained will vary from one to three months in individual cases, depending on the initial blood level. Treatment should be continued in full therapeutic doses for one month thereafter, in order to provide adequate stores of iron. In women past the menopause, maintenance treatment is in general not required, because of their decreased demands for iron. In individuals still menstruating a tendency to relapse is frequently present. If the periods are profuse or if pregnancy occurs, iron treatment on the lines laid down in the section devoted to Prophylaxis should be instituted. In those with normal or scanty periods it is unnecessary to continue iron treatment, provided that re-

without any obvious cause, such as pregnancy, post-partum hæmorrhage, abortion or infection, the most likely cause of the anæmia is menstrual blood loss. In some persons a clear history of menorrhagia is obtained, whereas in others the periods are stated to be normal. Little reliance, however, can be placed on a woman's assessment of her menstrual loss. If it is believed that excessive menstrual blood loss is occurring it is not sufficient merely to prescribe iron, it is essential to exclude organic disease of the uterus or adnexæ, and to consider the question of endocrine dysfunction. Before advising curettage for menorrhagia in women already anæmic, the possibility of such diseases as thrombocytopenic purpura and leukæmia should be excluded and a course of iron therapy should be instituted, since correction of the anæmia not infrequently promotes normal periods. In other cases menstrual loss of blood may not be reduced or may even become more profuse. In such cases either curettage or endocrine treatment may be indicated. If the woman is approaching the climacteric, induction of the menopause by irradiation of the ovaries may be advisable.

Curative Treatment

Treatment may be considered under the following heads:

(*a*) General measures.
(*b*) Iron treatment.
(*c*) Dietetic treatment.
(*d*) Symptomatic treatment.

(*a*) **General Measures.**—These include the provision of physical and mental rest, fresh air and sunshine if possible, and the avoidance of chills. Ideally, if the hæmoglobin level is 40 per cent. or less, the patient should be confined to bed except for purposes of toilet. Frequently, however, the woman has no one to help her with household duties, and in these circumstances one must advise as much rest as possible until the hæmoglobin level has been raised by iron therapy. Since the hæmoglobin level and the blood volume fall very slowly in chronic nutritional hypochromic anæmia and in pernicious anæmia, the patients become, to a considerable extent, acclimatized to a low level of hæmoglobin and can often undertake moderate exertion with little disability. (This is in contrast to the state of shock which occurs in patients with a sudden external loss of blood, even though the hæmoglobin has fallen only to 50 or 60 per cent.) Nevertheless, until iron treatment has improved the anæmia, rest in bed is the best form of treatment for alleviating the symptoms of anoxæmia, circulatory instability and myocardial weakness, namely dyspnœa, palpitation, giddiness, etc. As the hæmoglobin level rises, the amount of exertion undertaken should be gradually increased, but if possible it should stop short of producing these symptoms.

(*b*) **Iron Treatment.**—It is now generally agreed (1) that iron is absorbed in the ferrous state mainly from the duodenum and upper jejunum and that ascorbic acid facilitates its absorption; (2) that the ferrous salts are more efficacious than similar doses of the ferric salts; (3) that preparations of iron in combination with protein, e.g. bone marrow and hæmoglobin are valueless; (4) that much larger doses of iron are necessary to produce optimal results than were formerly used; and (5) that parenteral iron therapy is seldom required.

With the scheme of dosage suggested above, untoward general reactions are unusual. Occasionally there may be some degree of collapse, and pain in the chest, back and limbs. The occurrence of a severe reaction of this type in any patient should contra-indicate the further use of intravenous iron.

An intramuscular preparation of iron is available as an iron dextran complex (Imferon, Benger's Ltd.). Each ampoule of 5 ml. contains 250 mg. of iron, but utilization is less complete than in the case of intravenous iron. Hence an injection of 5 ml. of Imferon produces only slightly greater hæmoglobin [illegible] slower with intramuscular than with intravenous therapy.

[illegible] outer quadrant of the buttock.

[illegible] out-patients, the first manifestation may not appear until the patient is at home. Adrenaline (5 to 10 min. subcutaneously) or an antihistamine drug such as Piriton Maleate (Allen and Hanbury's Ltd.), 10 to 20 mg. intramuscularly or intravenously, are of value in both the early and delayed reactions.

(*c*) **Dietetic Treatment.** In severely anæmic patients with anorexia, [illegible] ments for iron conditioned by pregnancy or menstruation cannot be satisfied by a maintenance diet containing this amount of iron, the administration of iron by mouth for one week in each month must be advised after the normal hæmoglobin level has been restored.

It should be pointed out that although, in general, diets rich in iron (20 to 25 mg. daily) are expensive, it is quite possible to prescribe a dietary regimen which will provide a moderate iron content of 10 to 15 mg. daily at quite low cost. Oatmeal, lentils and split peas are cheap sources of food iron, and if reasonable quantities of the flesh foods, eggs, bread and green vegetables are taken as well, the iron intake will be satisfactory. In addition, an improvement in the protein, mineral and vitamin content will result.

(*d*) **Symptomatic Treatment.**—When satisfactory iron therapy is undertaken, the hæmoglobin level rises and, as it does so, all the manifestations of chronic nutritional hypochromic anæmia rapidly disappear in the great majority of cases. This applies not only to gastro-intestinal symptoms (anorexia,

and the factors causing anæmia outlined in the section on Prophylaxis, are equally applicable to the prevention of relapse.

Parenteral Iron Therapy.—The oral administration of iron produces such satisfactory results that parenteral therapy is rarely indicated. It may be required for the anæmic patient who has a true intolerance to iron given orally, but it should be pointed out that, while patients are frequently referred to us by their family doctors with the statement that they cannot take any preparation of iron by mouth, explanation, persuasion and attention to the points mentioned in the preceding paragraphs successfully overcome the so-called intolerance in the great majority of cases. Parenteral iron therapy may also be required in the cases of hypochromic anæmia which fail to respond to adequate oral therapy with iron and vitamin C because of malabsorption or for reasons not understood. It should be emphasized, however, that such cases are rare. Lastly, when hypochromic anæmia of moderate or severe degree is discovered late in pregnancy, parenteral iron therapy may be used because it produces an increase in [illegible] efficacy of parenteral and oral iron therapy may lead to incorrect conclusions if cases are treated as out-patients. Our experience has been that it is impossible to be certain of the dosage of iron taken by mouth unless the patient is in hospital. Frequently patients who have been regarded as refractory to oral iron therapy as out-patients respond very satisfactorily to the same dose of the same preparation in hospital.

When the decision to give parenteral iron therapy has been taken, a choice has to be made between the preparations which are available for intravenous injection and those which are given intramuscularly. The main advantage of intramuscular iron is the ease with which it can be administered, but at present insufficient information is available to indicate whether it should supersede intravenous iron. Generally it may be said that the administration of iron by either route gives satisfactory results and that general reactions of an alarming nature are rare. In the paragraphs which follow, the main points about both types are given in detail.

Satisfactory preparations of intravenous iron are Ferrivenin (Benger's Ltd.), Iviron (British Schering Ltd.) and Neo-Ferrum (Crookes Laboratories Ltd.) Each is a 5 per cent solution of saccharated oxide of iron in sucrose. In 5 ml. there are 100 mg. elemental iron, and this amount may be expected to increase the hæmoglogin level by approximately 4 per cent, since it has been found that practically all the injected iron is used in the formation of new hæmoglobin It is usual to give 2 ml. on the first day and thereafter 5 ml. every second or third day until enough iron has been given to correct the initial deficiency of hæmoglobin This amount is easily calculated from the figures given above. Thereafter a further four to five injections are given to ensure replenishment of the body stores of iron It is probably wise to give no more than this amount until more precise information is available regarding the possible ill effects of excess iron in the tissues.

It is important that none of the solution be allowed to enter the subcutaneous tissues, otherwise local irritation is likely to occur. Avoidance of this complica- [illegible] the colour of the iron solution is dark brown [illegible] in has been

respond to the administration of vitamin C but not to iron, but in many cases of scurvy both iron and vitamin C are deficient and must be prescribed. In some cases of iron deficiency anæmia without frank manifestations of scurvy, but where the dietary history suggests the possibility of sub-clinical scurvy, a supplement of ascorbic acid may augment the hæmatinic effects of iron or may initiate a response which has not been produced by iron alone. It must be pointed out, however, that it is unnecessary to prescribe ascorbic acid in the great majority of cases of iron deficiency anæmia if a satisfactory diet is taken. Accordingly it is a wise practice to make sure that all cases of iron deficiency anæmia take a diet rich in vitamin C [illegible]

[illegible] be tried.

NUTRITIONAL HYPOCHROMIC ANÆMIA OF INFANCY AND CHILDHOOD

Since an adequate store of iron in the fœtal liver is of some importance in maintaining a satisfactory blood level in infancy, careful attention should be directed to the provision of a well-balanced diet for the pregnant mother, and the administration of iron should be undertaken if anæmia is present during pregnancy. Such measures are desirable not only from the point of view of prevention of anæmia in the infant but probably also as a means of improving its general nutrition.

A rapid fall in the hæmoglobin level occurs during the first two months of extra-uterine life. No method of treatment can prevent this fall, which appears to be physiological. Recovery normally occurs during the next eighteen months, but there are three factors of particular importance which may prevent or retard this improvement. The first of these is low birth weight occurring as a consequence of prematurity or otherwise. All children of low birth weight [illegible]

[illegible] rule. Since mild degrees of anæmia have been shown to be frequent in infants of the poorer classes between six and eighteen months, even in the absence of low birth weight and obvious infection, a third factor must be considered. It is probable that at this age-period nutritional factors are also of importance, namely, undue delay in the change from a milk to a mixed diet and the poor quality of the mixed diet which is given. Accordingly the practitioner would be well advised to institute iron therapy in all cases where the infant appears to be pale, easily fatigued and not thriving.

Iron.—A palatable, efficient and non-irritating preparation of iron in liquid form which can be added to the infant's feed is the ideal. For a child of three to six months, 0·1 g. (1½ gr.) of iron and ammonium citrate in water sweetened with glycerin, three times a day, is a satisfactory preparation for prophylactic use. The dose should be [illegible]

nausea, vomiting, constipation or diarrhœa) but also to glossitis, koilonychia, dysphagia and paræsthesiæ. It follows that symptomatic treatment is seldom necessary.

Gastro-intestinal Symptoms—If gastric upset is prominent in the early stages of treatment, beneficial results may follow the administration of an *alkaline mixture, i e. aluminium hydroxide mixture* (N.F.) a teaspoonful after meals or magnesium carbonate mixture (B.P.C.) a dessertspoonful after meals In other cases a teaspoonful of the mixture in a tumblerful of warm water should be taken on awakening in the morning and before going to sleep at night, with the object of loosening the excess of mucus in the stomach. Dilute hydrochloric acid has been used extensively in the treatment of dyspepsia and diarrhœa associated with achlorhydria. It is very unlikely that this treatment has any beneficial effects; and this is hardly surprising, since the amount of hydrochloric acid necessary to bring about a significant change in the *p*H of the gastric contents is many times greater than the pharmacological dose. Constipation may need appropriate treatment. Many doctors think that iron has a

Glossitis.—In the majority of cases there is atrophic glossitis with little or no pain, and regeneration of the epithelium may be expected to occur as a result of iron treatment. In some cases the tongue is red, inflamed and painful (acute generalized glossitis). In others, painful fissures or ulcers, and fissuring of the angles of the mouth (angular stomatitis) are present. These changes are probably due to a long-continued deficient intake of members of the vitamin B complex, especially nicotinic acid, riboflavin, pyridoxine and folic acid There can be no doubt that tongue changes can be produced in animals and in humans by a deficiency of these members of the vitamin B complex, but it is not clear whether one or a combination of several of these factors is, in fact, responsible for the glossitis in chronic nutritional hypochromic anæmia. A

a disappearance

supplement of

min B complex,

should be given. During the acute stage of glossitis the diet must be bland and fluid, and the use of a glass tube to enable the patient to take the food directly to the back of the pharynx may be helpful as a temporary expedient.

Dysphagia—A mild degree of dysphagia is not uncommon and requires no special treatment as it improves *pari passu* with the hæmoglobin level. If it is more severe and persistent, the passage of a mercury bougie may be necessary. In a small proportion of cases a mechanical cause is present, namely, a web occluding the inlet to the œsophagus. In such cases an œsophagoscope should be introduced and the membrane ruptured or cut.

Paræsthesiæ—Numbness and tingling in the extremities are common, and in the great majority of cases no special treatment is required, since the paræsthesiæ disappear as the hæmoglobin level rises. If they persist, it is probable that there is a deficiency of vitamin B complex, and this may be corrected by

5 mg. of

necessary

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respond to the administration of vitamin C but not to iron, but in many cases of scurvy both iron and vitamin C are deficient and must be prescribed. In some cases of iron deficiency anæmia without frank manifestations of scurvy, but where the dietary history suggests the possibility of sub-clinical scurvy, a supplement of ascorbic acid may augment the hæmatinic effects of iron or may initiate a response which has not been produced by iron alone. It must be pointed out, however, that it is unnecessary to prescribe ascorbic acid in the great majority of cases of iron deficiency anæmia if a satisfactory diet is taken. Accordingly it is a wise practice to make sure that all cases of iron deficiency anæmia take a diet rich in vitamin C.

[illegible] be tried.

NUTRITIONAL HYPOCHROMIC ANÆMIA OF INFANCY AND CHILDHOOD

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A rapid fall in the hæmoglobin level occurs during the first two months of extra-uterine life. No method of treatment can prevent this fall, which appears to be physiological. Recovery normally occurs during the next eighteen months, but there are three factors of particular importance which may prevent or retard this improvement. The first of these is low birth weight occurring as a consequence of prematurity or otherwise. All children of low birth weight should receive iron therapy from the second month. The second indication for prophylactic iron therapy in infancy is the presence of an infection. Even a mild infection in infants may cause anæmia and retard blood regeneration—hence the administration of iron for some weeks following infection is a sound general rule. Since mild degrees of anæmia have been shown to be frequent in infants of the poorer classes between six and eighteen months, even in the absence of low birth weight and obvious infection, a third factor must be considered. It is probable that at this age-period nutritional factors are also of importance, namely, undue delay in the change from a milk to a mixed diet and the poor quality of the mixed diet which is given. Accordingly the practitioner would be well advised to institute iron therapy in all cases where the infant appears to be pale, easily fatigued and not thriving.

Iron.—A palatable, efficient and non-irritating preparation of iron in liquid form which can be added to the infant's feed is the ideal. For a child of three to six months, 0·1 g. (1½ gr.) of iron and ammonium citrate in water sweetened with glycerin, three times a day, is a satisfactory preparation for prophylactic use. The dose should be 0·2 g. (3 gr.) three times a day if anæmia has already developed. For children of six to eighteen months the prophylactic dose is 0·2 g. (3 gr.) while the curative dose varies from 0·3 to 0·6 g. (5 to 10 gr.) three

daily. The ferrous salts of iron have been shown to have a higher percentage utilization than the scale preparations, and in our opinion are preferable, since they are equally efficacious in smaller doses. It must be remembered that their efficiency is rapidly reduced if oxidation to the ferric state occurs. Accordingly they must not be prescribed in simple watery solutions but should be mixed with 50 per cent glucose, which retards oxidation (see p. 242). Whatever preparation of iron is used, treatment should be started by giving doses of one-third to one-half of what is ultimately desired, and the material should be mixed with the feed or given at the end of a feed.

Copper, manganese and some other minerals are believed by certain workers, on the basis of laboratory research in animals, to be necessary for normal hæmopoiesis. Of these minerals the claims of copper alone may be said to have received complete acceptance It promotes the full utilization of iron in the formation of hæmoglobin by a catalytic action. Because only traces are required it is extremely doubtful if there is any need for its addition to preparations of iron, since our investigations have shown that even in the diets of the poorest classes adequate quantities are present for this purpose. Should the practitioner desire to give copper as well as iron, certain proprietary preparations are available, such as the ferrous sulphate tablets marketed under the name of Fersolate by Glaxo Laboratories, which contain traces of copper and manganese. The difficulty of giving iron in tablet form to infants may be overcome by crushing the tablet in a little warm water immediately before use and mixing it with a feed.

Parenteral iron therapy may be indicated in infants with a true intolerance for oral iron or when it is clear that the mother is not carrying out the treatment recommended. Intramuscular iron (Imferon) is to be preferred to intravenous iron because of the scarcity of veins of suitable size in infants. It is usual to inject 1 ml., which contains 50 mg of iron, at intervals of two or three days. If the anæmia is moderate (Hb. 60 to 70 per cent.) three or four such injections suffice to bring the hæmoglobin level to normal; if it is severe (Hb about 30 per cent.), about ten injections are needed Reactions are said to be rare if these doses are not exceeded.

IRON DEFICIENCY ANÆMIA IN MEN

In the majority of cases chronic blood loss is the cause, and investigation and treatment should follow the lines laid down on p. 402. If blood loss can be excluded, the possibility of idiopathic steatorrhœa should be kept in mind and, if necessary, fat balance studies may be done. There is good evidence, however, that hypochromic anæmia is seen occasionally in late adolescence and early adult life which cannot be attributed to either of the causes mentioned. Probably it is produced by a combination of two factors: (1) deficient iron intake due to faulty diet, and (2) increased requirements for iron due to rapid growth in childhood and adolescence. Sometimes achlorhydria is present as well and plays a contributory role by reducing the absorption of iron. Treatment is on the same lines as for chronic nutritional hypochromic anæmia of women, but since the demands for iron in adult men are very low in the absence of external blood loss, it is seldom that treatment will have to be continued after the diet has been corrected and the anæmia has been cured by iron therapy.

POST-HÆMORRHAGIC ANÆMIA

Extravascular blood loss may be acute or chronic. It is necessary to describe the treatment of these two conditions separately, because the mechanism of their symptomatology and the treatment are entirely different.

ACUTE POST-HÆMORRHAGIC ANÆMIA

[illegible]
of l [illegible]
[illegible]
of l [illegible]

Arrest of Hæmorrhage.—In some cases hæmostasis may be secured by ligature of or pressure on the bleeding point—for example, a severed artery, extra-uterine gestation or the bursting of a superficial varicose vein. In other cases, such as in hæmorrhage from a peptic ulcer, it may be possible to ligate the ruptured vessel, but usually this procedure is not indicated. Lastly, the hæmorrhage may be part of a general blood disease such as thrombocytopenic purpura, hæmophilia or acute leukæmia, where mechanical arrest of the hæmorrhage may be impossible.

Treatment of Shock.—The degree of shock which follows a sudden loss of blood depends on several factors. The principal ones are the amount and rate of blood loss, the age and previous health of the patient and, in accidents and major operations, the concomitant effects of tissue trauma and previous exposure to cold. Since the decision to give intravenous fluids depends on a proper appreciation of these factors, it is desirable that they should be elaborated.

The sudden loss of 500 ml. of blood will not produce symptoms of shock in a healthy adult, as is clearly indicated from everyday experience with blood donors. When symptoms arise, they are usually psychological in origin rather than the result of lowered blood volume. Definite symptoms of shock appear when 1,000 ml. of blood is lost rapidly and a fatal result may occur if the figure approaches 2,000 ml. If the loss is spread over twenty-four hours, the symptoms are less severe and the prognosis correspondingly better. Infants and old people stand acute hæmorrhage relatively badly, and this is particularly true if there is a history of previous debility or ill-health.

A patient suffering from acute post-hæmorrhagic anæmia and shock should immediately be placed in bed between blankets. A suitable dose of morphine should be injected subcutaneously and repeated in two hours if necessary. The amount required is the minimal quantity necessary to allay apprehension and restlessness, and to control pain if present. Excessive doses of morphine are harmful because of its depressant effect on the respiratory centre. For an adult 15 mg. ($\frac{1}{4}$ gr.) and for a child 5 to 10 mg. ($\frac{1}{12}$ to $\frac{1}{6}$ gr.) is sufficient for the initial dose. The foot of the bed should be raised on blocks, the patient being kept flat on his back except for a low pillow under his head. In severely exsanguinated patients awaiting blood transfusion, the limbs should be bandaged with crêpe bandages from below upwards. The body heat should be restored by placing hot bottles along both sides of the body, due care being taken not to burn the patient, whose threshold for pain may be raised owing to collapse, by ensuring that the bottles are well covered by flannel and are not too hot. When available, a radiant heat cradle should be used, as a more even warming of the body can be obtained without the danger of burning the patient. The

temperature should be controlled so as to avoid cutaneous vasodilatation and excessive sweating, which would increase the fluid loss and thus further deplete the blood volume. Cardio-respiratory stimulants are frequently ordered for patients with severe collapse while awaiting the assembly of the apparatus necessary for intravenous transfusion. Pituitary extract, strychnine, nikethamide and methedrine have been used for this purpose. Consideration of the mechanics of the circulation in post-hæmorrhagic shock suggests that these drugs are unlikely to be of value and may actually be harmful. As a compensation for blood loss, widespread vasoconstriction occurs spontaneously in an attempt to maintain the blood pressure at a level which will ensure adequate blood supply to the vital centres. Accordingly there appears to be little object in giving the vasoconstrictor drugs adrenaline and posterior pituitary extract. Likewise, injections of nikethamide and strychnine are unlikely to be helpful, since the cardiovascular and respiratory centres of the brain are already doing their utmost to maintain a satisfactory circulation and respiratory exchange.

Since the essential cause of shock in acute hæmorrhage is the resulting low blood volume, the restoration of the blood volume is undoubtedly the most important therapeutic procedure required. When shock is only mild in degree, all that may be necessary is an adequate amount of water by mouth. One pint of fluid per hour, for three or four hours, may make good the deficiency. If the [illegible] technique [illegible] or recon- [illegible] nentioned, blood must take first preference, since it is of the correct viscosity and osmotic pressure and the contained corpuscles effectively increase the oxygen-carrying capacity. Second in order of merit is plasma or serum. If none of these is available, dextran (6 per cent. in normal saline) should be used, because it holds the fluid within the vessels for a considerable time. On the other hand, saline and glucose saline pass out of the blood and into the tissue spaces within a few minutes of their injection and hence cannot be recommended for the restoration [illegible] the dehydr[illegible] diarrhœa. [illegible] volume by approximately 7 per cent., with a concomitant increase of blood volume and of blood pressure. One, two or more pints of blood should be introduced, the amount depending on the severity of the shock and the degree of anæmia present. Similar quantities of plasma or dextran are indicated if blood is not available.

Blood transfusion should preferably be given by the continuous drip method, as by this means 2,000 to 3,000 ml. (3·5 to 5 pints) of blood can be introduced over twenty-four hours with complete restoration of the blood volume and with the lowest possible risk of producing acute heart failure and pulmonary œdema, or causing aggravation or recurrence of the hæmorrhage due to a sudden increase in the blood pressure. In a healthy person suffering from hæmorrhagic shock as the result of an accident or a wound, the first pint (0·57 [illegible]

available even if the initial degree of shock is not marked, since recurrence or increase in the severity of the hæmorrhage may suddenly precipitate the patient into a dangerous state of collapse. Moreover, it is wise, especially in cases of hæmorrhage from the alimentary tract, to consult a surgeon before the state of severe collapse has developed. In this way operation may be carried out with less delay if recurrent hæmorrhage should make it necessary.

It is now necessary to discuss the indications for blood transfusion. It is unwise to rely solely or mainly on a blood count, since for some hours after acute hæmorrhage the hæmoglobin and red cells per c.mm. of blood may be little altered. Moreover, a falling hæmoglobin level does not necessarily prove that hæmorrhage is continuing. Accordingly an estimation of the degree of shock with its concomitant fall in blood volume should be based on the following clinical signs: a rising pulse rate (½ hourly chart) and a progressive fall in blood pressure, sighing respiration, uneasiness and restlessness, coldness and clamminess of the skin, pallor, general weakness and impairment of mental faculties. When the pulse rate is over 100 per minute and the systolic blood pressure below 90 mm. Hg, a considerable degree of shock is present. It has been calculated that the blood volume is less than 60 per cent. of normal when the systolic blood pressure falls below 80 mm. Hg, and the prognosis is very grave unless immediate blood transfusion is given.

It should be remembered that the great upset in the dynamics of the circulation which occurs following severe hæmorrhage necessitates the continuation of complete rest in the recumbent position, warmth and good nursing for at least a week after restoration of the blood volume. Thereafter treatment comprises removal of the causal condition where possible and the application of the measures already given in detail in the section devoted to chronic nutritional hypochromic anæmia under the headings General Measures, Iron and Diet (p. 402).

CHRONIC POST-HÆMORRHAGIC ANÆMIA

The treatment of chronic blood loss is considered under two headings: (*a*) Removal of the Causal Condition, and (*b*) Treatment of the Anæmia.

(*a*) **Removal of the Causal Condition.** The most frequent cause of this form of anæmia, especially in males, and the one most likely to be missed, is occult bleeding from the gastrointestinal tract. We have not infrequently seen patients with hæmoglobin levels below 30 per cent. who were unaware that they were losing blood by this route. The occult bleeding may come from varicose veins in the œsophagus and stomach, peptic ulcers of stomach or duodenum, malignant tumours or polypi of the gastrointestinal tract, hæmorrhoids or infestation with animal parasites, particularly ankylostomata. Attention is drawn to the great value of the benzidine reaction for the recognition of occult blood in the stools. More obvious causes of chronic blood loss are excessive hæmorrhage from the uterus resulting from the presence of tumours, polypi or endocrine dysfunction, repeated nose-bleedings, and chronic blood diseases such as purpura, hæmophilia and scurvy. In the great majority of cases of obscure hypochromic anæmia the gastro-intestinal and urogenital tracts should first be investigated as possible sources of hæmorrhage. When the cause of the hæmorrhage has been discovered treatment directed to its removal must be instituted. It should be noted that the diet frequently prescribed for diseases of the gastrointestinal tract

is often low in iron and vitamin C and may accentuate the anæmia if these deficiencies are not corrected.

(*b*) **Treatment of the Anæmia.** This consists of the administration of full doses of iron, together with the general measures outlined under chronic nutritional hypochromic anæmia (see p. 402) If the source of bleeding has been removed, the chances of relapse after the blood count has been brought to normal are insignificant and therefore, in general, maintenance treatment with iron is not required.

PERNICIOUS ANÆMIA AND OTHER MEGALOBLASTIC ANÆMIAS

It is necessary to emphasize that there are many types of macrocytic anæmia which differ widely one from another in their ætiology, blood picture and response to treatment. We believe it is preferable to replace the term megalocytic anæmia by megaloblastic anæmia. The term " macrocytic " could then be used to cover all anæmias characterized by an increased mean cell diameter, including the " megaloblastic " group. If this is accepted, it is possible to [illegible]

[illegible]

group of relatively rare macrocytic anæmias resulting from widely differing causes. The macrocytosis is secondary, in the majority of cases, to prolonged stimulation or irritation of the bone marrow. Blood formation proceeds on a normoblastic basis, but owing to its excessive activity the parent cells in the bone marrow are primitive normoblasts and as a result many of their offspring entering the peripheral circulation are larger and less mature than normal erythrocytes

It is hoped that the preceding remarks make it clear that all megaloblastic anæmias, unless accompanied by iron deficiency, are macrocytic, but that all macrocytic anæmias are not megaloblastic. The following discussion will be restricted to the treatment of pernicious anæmia and other megaloblastic anæmias

CLASSIFICATION AND PATHOGENESIS OF THE MEGALOBLASTIC ANÆMIAS

A clinical classification of the megaloblastic anæmias is given on p 400 For a rational approach to treatment, however, a brief discussion of the patho- [illegible]

folinic acid (the citrovorum factor)

Cyanocobalamin.—The isolation of the active anti-pernicious anæmia principle in liver was announced simultaneously by British and American workers in 1948 It has been named cyanocobalamin in the British Pharma-

copœia and this name is used hereafter in this chapter. Cyanocobalamin is clinically active in amounts as small as 1 microgram daily. It is a red substance containing cobalt and its formula is now known. It has no chemical relationship to either folic or folinic acid. The cost of preparing the material from liver was so great that it was likely that the discovery would be of no clinical importance unless the substance could be synthesized or isolated more cheaply by other methods. The discovery that the culture medium in which *Streptomyces griseus* grows is a rich source of cyanocobalamin has enabled its production to be undertaken on a large scale at low cost. The active principle in purified liver extract is now known to be cyanocobalamin, and trials have clearly shown that its therapeutic efficacy is identical with that of highly purified liver extract in every respect, including the capacity to prevent the onset of subacute combined degeneration of the cord, and to benefit or cure the neurological features if already present prior to the commencement of treatment. The cost of cyanocobalamin is considerably less than purified liver extracts. Its other advantages are that the bulk of fluid to be injected is small, namely 1 ml., and that it produces no allergic reactions, being a protein-free product. For these reasons cyanocobalamin has replaced parenteral liver therapy in pernicious anæmia and no further mention will be made of purified liver extracts. The writers suggest [illegible] tenance treatment can only be found by trial in each individual case, but it is suggested that the average requirements will be 100 micrograms every two, three or four weeks. Inhalation of cyanocobalamin in the form of a snuff, or its oral ingestion combined with intrinsic factor, are methods of administration which are unreliable for therapeutic purposes.

Folic Acid.—The name "folic acid" was originally given to a substance isolated from spinach. It has been shown to be present in the green leaves of other plants and also in mushrooms, yeast and in animal tissue such as liver and kidney. Folic acid is a member of the vitamin B complex and is an essential factor required for the growth of certain bacteria such as the *Lactobacillus casei* and for the normal growth and development of a variety of animals. The chemical name for folic acid is pteroylglutamic acid. In 1946 synthetic folic acid was marketed by the Lederle Company of America under the trade name Folvite. It is supplied in ampoules for parenteral injection and in tablets for oral ingestion. Each tablet contains 5 mg. of folic acid. The suggested initial dose for the treatment of all types of megaloblastic anæmia other than pernicious anæmia is 10 to 20 mg. daily for ten days and 5 mg. daily thereafter until the blood count is normal. For maintenance treatment the requirements have not been finally established. Probably they lie in the region of 2·5 to 5 mg. daily. There is no object in using the parenteral route, as oral administration is simpler and probably more effective, except possibly in the malabsorption syndrome when an intramuscular injection of folic acid may be given for two or three days at the start of treatment. We have given folic acid in a single dose of 0·4 g. by mouth and 0·2 g. by intramuscular injection. No unpleasant reactions were produced and an excellent hæmopoietic response resulted. Large single doses are, however, wasteful and extravagant, since their effect in raising the blood level continues only for about two or three weeks and a much larger gain

in red cells and hæmoglobin can be obtained if the same amount of material is given in divided doses of 5 to 10 mg. daily.

Folinic Acid, or the citrovorum factor, is a substance which is chemically related to folic acid, and is necessary for the growth of a streptococcus named *Leuconostoc citrovorum*. It is probable that folic acid obtained from food is altered in the body to folinic acid, and *it is possibly in this form that folic acid* accomplishes its metabolic function. Folinic acid has been shown to be effective in the treatment of Addisonian pernicious anæmia, the megaloblastic anæmia of pregnancy and the sprue syndrome in doses of the same order as those recommended for folic acid. Folinic acid is not available commercially, but this is of no importance, since it is not more active than folic acid.

It is probable that cyanocobalamin, folic acid and folinic acid all play some essential but little understood role in the metabolism of nucleic acid and that all three factors are required for the continuation of normoblastic blood formation. Although the inter-relationship between these factors has not yet been finally determined, the therapeutic indications for their employment are already clearly established. Thus in Addisonian pernicious anæmia, cyanocobalamin is the drug of choice because here the development of megaloblastic blood formation is a direct consequence of defective assimilation of this vitamin. This results from a failure of production by the stomach of the intrinsic factor of Castle which is now believed to be essential for the absorption of cyanocobalamin. On the other hand, in the megaloblastic anæmias of pregnancy and infancy, in nutritional (tropical) megaloblastic anæmia, in most cases of the malabsorption syndrome and in idiopathic refractory megaloblastic anæmia, including achrestic anæmia, folic acid is the drug of choice, since these anæmias are essentially nutritional in origin, being related to defective intake or malabsorption of the conjugates of folic acid. In favour of this view is the fact that the megaloblastic anæmias, other than Addisonian pernicious anæmia, are frequently partially or completely refractory to cyanocobalamin, but invariably respond to folic acid. It should be pointed out that in Addisonian pernicious anæmia folic acid should *not* be prescribed because of its inability to prevent the development of subacute combined degeneration of the cord. Lastly, it should be remembered that in the megaloblastic anæmias a dual deficiency of iron and folic acid or cyanocobalamin is often present In these circumstances, after carefully reviewing the response to cyanocobalamin or to folic acid, iron therapy may be started (see p 404) The essential indication is that the rapid production of red cells has outstripped the supply of hæmoglobin, and this is shown by the development of hypochromic anaemia.

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The decision is often a difficult one to make. Undoubtedly blood transfusion in such severely anæmic patients should not be undertaken without a full realization of the risks involved, the most important of which is the possible occurrence of acute pulmonary œdema and death. This catastrophe is due to a failure of the weakened myocardium to withstand the effects of the increase in blood volume which accompanies transfusion. Accordingly we believe that transfusion of concentrated red cell suspension (that is, citrated blood from which most of the plasma has been removed) is better than the use of whole blood. In this way the number of red cells in the circulation may be increased with relatively little increase in the blood volume. The packed red cells should be transfused very slowly, one pint (i.e. the red cells derived from approximately two pints of blood) being given in not less than six hours, or one half-pint given in not less than two hours on each of two successive days. In less urgent cases, in which some doubts exist regarding the need for immediate transfusion, the patient's blood group should be determined so that a transfusion can be given without delay should the necessity arise.

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Hog's stomach preparations are insoluble and contain the gastric enzyme (Castle's intrinsic factor), which is thermolabile, hence they must not be heated. While excellent results can be obtained from the use of commercial preparations of desiccated stomach in a dose of 1½ oz. daily, they are not recommended for routine use for the same reasons which apply to oral liver therapy. Folic acid must not be used for the treatment of Addisonian pernicious anæmia, for it does not prevent the onset of subacute combined degeneration of the cord and may even accelerate its production. Within two or three days the reticulocyte increase will have started and a marked subjective improvement will be noted. A weekly injection of 100 micrograms of cyanocobalamin should be given until the red-cell count is normal. It not infrequently happens that the blood level [illegible] as arteriosclerosis or chronic sepsis and hæmorrhage. It is essential to restore the blood level completely to normal (5 million red cells and 100 per cent. hæmoglobin), as this is important in preventing degenerative changes in the

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ccurrence of acute pulmonary œdema and death. This catastrophe is due to a
ilure of the weakened myocardium to withstand the effects of the increase in
lood volume which accompanies transfusion. Accordingly we believe that
ansfusion of concentrated red cell suspension (that is, citrated blood from which
ost of the plasma has been removed) is better than the use of whole blood.
n this way the number of red cells in the circulation may be increased with
elatively little increase in the blood volume The packed red cells should be
ansfused very slowly, one pint (i e. the red cells derived from approximately
wo pints of blood) being given in not less than six hours, or one half-pint given

[illegible]

When the diagnosis of pernicious anæmia has been established, an intra-
uscular injection of 100 micrograms of cyanocobalamin should be given and
epeated in twenty-four hours Parenteral treatment with purified liver extracts
s no longer recommended for the reasons given on p 415 Liver, or liver
xtract by mouth, was the treatment of choice prior to 1932 Oral treatment can
no longer be recommended, because it is more expensive and less effective than
parenteral therapy. In addition, experience has shown that many patients fail
o continue to take the amount required to attain and maintain a normal blood
evel owing to the nausea and disgust engendered by the constant sight, taste
and smell of the liver or liver extract.

[illegible]

even accelerate its production. Within two or three days the reticulocyte

[illegible]

as arteriosclerosis or chronic sepsis and hæmorrhage It is essential to restore
the blood level completely to normal (5 million red cells and 100 per cent.
hæmoglobin), as this is important in preventing degenerative changes

spinal cord, and it may be necessary at this stage to double or treble the number of weekly injections before recovery is complete.

A preparation of iron (see p. 405) should be given twice a day after meals and continued for two months in all cases receiving treatment by the parenteral route, since an iron shortage is apt to arise owing to the exceedingly rapid production of erythrocytes. Iron may increase the anorexia and dyspepsia so frequently present in the severe relapse stage of pernicious anæmia, and accordingly the administration should be delayed till after the occurrence of the reticulocyte crisis, by which time the marked clinical improvement of the patient will enable it to be well tolerated.

Hydrochloric acid, combined with glycerin of pepsin, is commonly prescribed if dyspepsia or diarrhœa is present. For the reasons stated on p. 408 it is of doubtful value.

It should be pointed out that the most efficacious treatment for all the symptoms of pernicious anæmia and for the prevention of such serious complications as spinal cord degeneration and disease of the gall-bladder is the parenteral administration of cyanocobalamin. Dyspepsia, diarrhœa, sore tongue and general weakness all disappear in the majority of cases without any symptomatic treatment.

The recommendations in regard to diet, nursing, rest, etc., for iron deficiency anæmia are equally applicable to pernicious anæmia (see pp. 403-409 for full details). If there is reason to suspect a deficiency of vitamin C, ascorbic acid, 50 mg. thrice daily, should be given for a fortnight, as there is evidence to show that such a deficiency may retard or even inhibit the response to cyanocobalamin.

Pre-operative Measures.—Should an emergency arise during the relapse stage of pernicious anæmia requiring an operation which cannot be delayed, intensive parenteral treatment should be undertaken immediately (100 micrograms cyanocobalamin intramuscularly, repeated after twelve hours) and preparations for blood transfusion made so that it can be given immediately if required. Patients in the remission stage of pernicious anæmia, particularly if they show signs of neurological disease, should receive double the usual quantity of cyanocobalamin for a few days before undergoing any major operation, since the blood level tends to fall and neurological degeneration to progress after serious surgical procedures.

Chronic focal sepsis (in tonsils, teeth or accessory sinuses) should not be treated radically until there has been an adequate response to specific anti-anæmic therapy. On the other hand, localized and easily accessible collections of pus should be promptly evacuated, since they tend to inhibit or retard the therapeutic response.

Maintenance Treatment.—Since cyanocobalamin does not produce a cure but is a form of substitution therapy, maintenance treatment must be continued for life This point should be carefully explained to patients, who will then be more likely to report regularly for the necessary treatment; and it should be noted also by all doctors, because, as we have found, some are liable to reduce or stop treatment after a remission has been induced.

The amount of cyanocobalamin required to maintain a normal blood level varies greatly in different individuals, often for no apparent reason. Only by trial, checked by blood counts, can the problem of dosage be satisfactorily settled. For maintenance treatment the necessary number of injections of cyanocobalamin varies in different individuals from one a week to one every six weeks.

In our experience an average dose is 100 micrograms of cyanocobalamin at intervals of approximately three weeks. Iron is not required if it has already been prescribed during the first two months of treatment. An ordinary well-balanced mixed diet is all that is necessary. Maintenance treatment with parenteral liver extracts, oral liver preparations or hog's stomach is not recommended.

SUBACUTE COMBINED DEGENERATION OF THE SPINAL CORD

Prophylaxis.—Lesions of the cord rarely if ever develop in pernicious anæmia if the blood level is maintained within normal limits. It must be emphasized, however, that the symptoms of a patient having maintenance treatment for pernicious anæmia cannot be relied upon as an indication of the blood level. Many patients receiving inadequate maintenance therapy have no symptoms although the blood count may be subnormal, e.g. Hb. 80 per cent, R.B.C. 3.5 to 4 million. It is in such cases that the incidence of subacute combined degeneration of the cord is highest. It is of great importance, therefore, that blood counts should be done at regular intervals (preferably every three months) during maintenance treatment, unless the expensive policy of giving excessive amounts of liver extract or cyanocobalamin is followed. If the red-cell count falls below 4.5 million in the case of women or 5 million in men, or if examination of a blood film shows the presence of macrocytes although the blood count is above those levels, maintenance treatment is inadequate and should, therefore, be increased. Our experience has convinced us that the danger of degeneration of the spinal cord is greatly reduced by observance of these precautions. The danger of spinal cord lesions developing when folic acid is employed as the sole therapeutic agent for initial and maintenance treatment is referred to on p. 416. In addition it is essential that patients with pernicious anæmia should not take proprietary preparations of vitamins or iron which contain folic acid.

Treatment.—The treatment of established subacute combined degeneration is mentioned in the section devoted to diseases of the nervous system (see p. 836). All that need be said here is that cases of pernicious anæmia with signs of neurological involvement should receive two to three times as much cyanocobalamin as those with a comparable blood picture but without neurological changes. This intensive treatment should be continued for at least six to twelve months after the blood count has reached normal and should be combined with remedial exercises. By these means many patients who are bedridden may be able to lead a useful life, while those with less severe involvement of the spinal cord may return to full employment. The failure of folic acid to prevent subacute combined degeneration is discussed on p. 416.

MEGALOBLASTIC ANÆMIAS OTHER THAN ADDISONIAN ANÆMIA

In other forms of megaloblastic anæmia the scheme of treatment outlined above may require modification with reference to the replacement of parenteral therapy with cyanocobalamin by folic acid or rarely by oral liver preparations.

MEGALOBLASTIC (PERNICIOUS) ANÆMIA OF PREGNANCY

We prefer the term "megaloblastic anæmia of pregnancy" for this group to the commoner name "pernicious anæmia of pregnancy," because some cases

spinal cord, and it may be necessary at this stage to double or treble the number of weekly injections before recovery is complete.

A preparation of iron (see p. 405) should be given twice a day after meals and continued for two months in all cases receiving treatment by the parenteral route, since an iron shortage is apt to arise owing to the exceedingly rapid production of erythrocytes. Iron may increase the anorexia and dyspepsia so frequently present in the severe relapse stage of pernicious anæmia, and accordingly the *administration should be delayed till after the occurrence of the reticulocyte* crisis, by which time the marked clinical improvement of the patient will enable it to be well tolerated.

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We prefer the term " megaloblastic anæmia of pregnancy " for this group to the commoner name " pernicious anæmia of pregnancy," because some cases

have a colour index of unity or slightly below, and the feature common to all the cases is a megaloblastic bone marrow.

While a minority of cases respond satisfactorily to injection of cyanocobalamin in doses similar to those required in Addisonian pernicious anæmia, the majority fail to respond, or do so only after a variable period during which blood transfusions may be necessary to maintain life. Satisfactory remissions can usually be induced in these cases by *the ingestion of 10 mg. daily of folic acid.* A deficiency of iron is also usually present and accordingly iron should be prescribed simultaneously with folic acid. Treatment can be discontinued after the puerperium and the restoration of a normal blood level.

Megaloblastic (Pernicious) Anæmia of Infancy

The disease is exceedingly rare The ætiological factors appear to be dietary deficiency, especially of ascorbic acid, with or without superadded infection, usually of the alimentary tract All cases treated with folic acid responded satisfactorily, including some which were refractory to the parenteral injection of liver extract and cyanocobalamin. Maintenance treatment is not required if the dietetic errors are corrected Iron and ascorbic acid may have to be given after the initial response to folic acid, as a deficiency of these two factors is frequently present. The condition is not related to cœliac disease.

Megaloblastic Anæmias due to Disorders of the Gastro-intestinal Tract

Radioactive techniques for the determination of cyanocobalamin absorption, and microbiological methods for the assessment of folic acid absorption and serum cyanocobalamin levels, have contributed greatly to an understanding of the megaloblastic anæmias due to disorders of the gastro-intestinal tract and have led to a more rational therapeutic approach. Broadly speaking, the causes of these anæmias can be classified into three main groups, viz.

1 Where there is impaired absorption of cyanocobalamin secondary to intrinsic factor deficiency arising from loss of or damage to the gastric mucosa

Total gastrectomy invariably produces a megaloblastic anæmia provided the patient lives long enough. In rare instances megaloblastic anæmia may follow partial gastrectomy or gastroenterostomy, in these cases secretion of intrinsic factor fails as a result of damage to the gastric mucosa from a spreading gastritis originating at the site of the anastomosis. By the same mechanism chronic gastritis associated with other conditions such as long-standing iron-deficiency anæmia and chronic alcoholism may occasionally give rise to a megaloblastic anæmia. Treatment of this group is exactly the same as for Addisonian pernicious anæmia (p. 416).

2 Where the main defect is in the absorption of folic acid as a result of

(*a*) a functional defect in the mucosa of the small intestine, i.e. sprue syndrome (tropical sprue, idiopathic steatorrhœa and cœliac disease);

(*b*) extensive organic disease involving the wall of the small intestine or its lymphatic drainage system, e.g. tuberculous enteritis, tabes mesenterica, regional ileitis, reticuloses and Whipple's disease.

Folic acid, in a dose of 10 to 20 mg. daily by mouth, causes reversal of the bone marrow to normoblastic erythropoiesis and a rapid improvement in the blood picture In cases with severe anæmia, initial parenteral treatment for

...ended Maintenance

...ological relapse

...robably around

...acid absorption

...ely as severe as

in the blind or stagnant loop

...ter a monthly injection of 100

...beneficial effects are ...

condition is usually much less satisfactory ... disease the anæmia is usually hypochromic and the bone marrow frankly normoblastic, so that treatment with iron is indicated. Folic acid fails to improve the clinical state or the anæmia except in the occasional case in which the bone marrow is megaloblastic.

... case of the malabsorption syndrome the causation of the under- ... appropriate treat- ...

culous enteritis and tabes mesenterica ... ...ic steatorrhœa a gluten-free diet may not only result in an improvement in the steatorrhœa and in the patient's general nutrition but may also produce a definite hæmatological response

3 Where the main factor is decreased availability to the body of cyanocobalamin

In Great Britain this arises as the result of destruction or utilization of cyanocobalamin by an abnormal bacterial flora in blind or stagnant loops of small intestine These anomalies may result from short-circuiting operations, fistulæ or strictures involving the small intestine, jejunal diverticulosis can produce similar effects, the diverticula constituting small stagnant pockets. Steatorrhœa occurs in a considerable proportion of cases with the stagnant loop syndrome As might be expected from the bacterial ætiology, the oral administration of a broad spectrum antibiotic such as *chlortetracycline* produces a hæmatological response which is often of considerable diagnostic value. The duration of the hæmatological response is extremely variable. When relapse occurs, subsequent courses of antibiotics may prove ineffective due to the development of bacterial resistance. For these reasons it is recommended that the megaloblastic anæmia of the blind or stagnant loop syndrome be treated by the parenteral administration of cyanocobalamin in the same manner as for Addisonian pernicious anæmia (p. 417). Folic acid therapy is rarely needed in

this group. Since the primary deficiency is of cyanocobalamin, folic acid must never be given alone because of the known danger of precipitating subacute combined degeneration of the cord. Where possible, surgical correction of the intestinal abnormality should be undertaken, since it may result in permanent cure of the anæmia and any existing diarrhœa and steatorrhœa. On the other hand, if surgical treatment is not feasible, e g. widespread jejunal diverticulosis, short courses of chlortetracycline at suitable intervals are often of value in improving the diarrhœa and steatorrhœa. An analagous syndrome occurs from infestation with the fish tapeworm, in this instance it is the parasite which destroys or utilizes cyanocobalamin. Treatment consists of expulsion of the worm with an anthelminthic and the correction of the anæmia with cyanocobalamin. If re-infestation does not occur, maintenance treatment with cyanocobalamin will not usually be required.

Nutritional Megaloblastic Anæmia

In many parts of the world, both tropical and non-tropical, a megaloblastic [illegible]

response, it is believed that the primary cause of this form of megaloblastic anæmia is a deficiency of folic acid in the diet and not usually a deficiency of cyanocobalamin. In keeping with these views is the finding that many cases are partially or completely refractory to the parenteral injection of purified liver extracts or cyanocobalamin. Wills obtained good therapeutic responses from autolyzed yeast products (Marmite) and crude liver extract (Campolon); liver and oral liver extracts are also effective. The treatment of choice, however, is folic acid in doses of 10 to 20 mg. daily, because of its effectiveness and ease of administration. Iron may be needed to correct an independent iron-deficiency anæmia If the diet is made adequate in all respects, maintenance treatment with folic acid and iron will not be required The absence of steatorrhœa distinguishes the condition from the sprue syndrome. It is necessary to point out that nutritional anæmia due to iron deficiency is infinitely more common than megaloblastic nutritional anæmia, and that such cases will respond only to iron and not to cyanocobalamin or folic acid Sternal marrow examination may sometimes be required to differentiate the two conditions in tropical countries because macrocytosis may be present even if the anæmia is primarily due to a deficiency of iron. The macrocytosis may possibly be due to the presence of reticulocytes, which are frequently found in increased numbers in patients suffering from chronic malaria and hookworm infestation.

Macrocytic Anæmia of Hepatic Disease

Megaloblastic blood formation is very rarely seen in patients with hepatitis; the macrocytic blood picture is more often associated with a macro-normoblastic bone marrow It is not surprising, therefore, that treatment with cyanocobalamin or folic acid is usually ineffective. Moreover, the prognosis depends not so much on the severity and type of anæmia present but on the degree and progress of liver damage. If treatment with iron, cyanocobalamin and folic acid fails, proteolyzed liver (see below) should be given a trial.

Idiopathic Refractory Megaloblastic Anæmia

[illegible]

which were not associated with pregnancy or due to malnutrition or malabsorption as judged by clinical, radiological and chemical investigations.

Included under this heading are the cases of megaloblastic anæmia named by Wilkinson "achrestic anæmia". The introduction of proteolyzed liver [illegible]

given orally. Because of its ease of administration, folic acid in doses of 10 to 20 mg. daily is the drug of choice.

Other Rare Megaloblastic Anæmias

(*a*) A megaloblastic anæmia develops in a small proportion of individuals harbouring the fish tapeworm (*Diphyllobothrium latum*). The worm utilizes the dietary cyanocobalamin at the expense of the host Expulsion of the worm will usually relieve the anæmia, but treatment should be supplemented with cyanocobalamin.

[illegible]

the administration of folic acid for as long as the anti-convulsant drug is *required*

Anæmia in Myxœdema

The anæmia of myxœdema is usually moderate in degree and normocytic or macrocytic in type. Accompanying iron deficiency is not uncommon The clinical picture may strongly suggest pernicious anæmia, but cyanocobalamin or folic acid therapy is usually ineffective, except in the very rare cases where a megaloblastic bone marrow is present. Administration of thyroid extract produces a slow improvement in the blood level Associated iron deficiency must be appropriately corrected.

HÆMOLYTIC ANÆMIAS

[illegible]

and an excess of immature circulating erythrocytes (reticulocytes) in the presence of a stationary or falling blood count. This term should not be applied to the mild hæmolytic phenomena which occur in the severe relapse stage of the megaloblastic anæmias, such as pernicious anæmia, sprue, etc In such diseases the anæmia is not mainly due to hæmolysis, but to disturbed erythropoiesis, whereas in the true hæmolytic anæmias hæmolysis is the essential factor in the production of the anæmia

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The hæmolytic anæmias comprise a group of anæmias of widely differing causation, *the essential diagnostic feature of which is the presence of excessive* blood destruction as demonstrated by the finding of bilirubinæmia, urobilinuria and an excess of immature circulating erythrocytes (reticulocytes) in the presence of a stationary or falling blood count. This term should not be applied to the mild hæmolytic phenomena which occur in the severe relapse stage of the megaloblastic anæmias, such as pernicious anæmia, sprue, etc In such diseases the anæmia is not mainly due to hæmolysis, but to disturbed erythropoiesis, whereas in the true hæmolytic anæmias hæmolysis is the essential factor in the production of the anæmia.

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splenectomy is performed and formation of calculi in the bile ducts may occur. On the other hand, if a chronically diseased gall-bladder with or without stones is found during an operation for splenectomy, the opportunity should then be taken to correct the biliary disease

Racial Hæmolytic Anæmias.—Sickle-cell anæmia, which occurs in negroes, is a very rare disease in Great Britain. Cooley's or Mediterranean anæmia (thalassemia major) is a rare familial condition almost exclusively limited to children of southern European stock. The defect is believed to lie

will be required in all severe cases Splenectomy is seldom indicated, as it usually does not alter the course of the disease. Occasionally when the spleen

HÆMOLYTIC ANÆMIAS DUE TO INFECTIVE OR TOXIC FACTORS

The treatment of this group differs widely from that of hæmolytic anæmia

fication of the conditions producing an infective or toxic hæmolytic anæmia facilitates an understanding of the problem

CLASSIFICATION

Infections and Intoxications.—Sepsis, streptococcal and staphylococcal septicæmia, gas gangrene (*Clostridium welchii* infection), malaria, Oroya fever.

In sepsis and in streptococcal and staphylococcal septicæmia it is now recognized that when severe anæmia develops it is in most cases due mainly to toxic inhibition of the bone marrow, and that a direct hæmolytic action, resulting from the bacterial infection, plays only a minor role in the production of the anæmia In gas gangrene, however, a severe anæmia may occur which is undoubtedly due to increased hæmolysis

Drugs and Industrial Hazards. e g lead, phenylhydrazine, potassium chlorate, the arsenicals, arseniuretted hydrogen (particularly in submarine

important to note that several cases of acute hæmolytic anæmia due to these drugs have been reported This complication is so rare, however, that it should not be considered a contra-indication to the employment of the drug in suitable cases.

TREATMENT

Removal of the Cause—In infections this may mean the evacuation of local collections of pus, the administration of antibacterial or antitoxic sera, or the

Hæmolytic anæmias are best classified as follows:

(*a*) Hæmolytic anæmia due to congenital abnormality of the erythrocyte.

1. Congenital hæmolytic anæmia (familial acholuric jaundice, hereditary spherocytosis)
2. The racial hæmolytic anæmias · sickle-cell anæmia and Cooley's anæmia.

(*b*) Hæmolytic anæmia due to infective, toxic or allergic factors.

(*c*) Hæmolytic anæmia due to hæmolysins.

1. Hæmolytic anæmia of the newborn (see p. 244).
2. Transfusion with incompatible blood (see p. 861).
3. Idiopathic (acquired) hæmolytic anæmia.
4. Symptomatic hæmolytic anæmia.
5. Paroxysmal hæmoglobinuria

HÆMOLYTIC ANÆMIA DUE TO CONGENITAL ABNORMALITY OF THE ERYTHROCYTE

Congenital Hæmolytic Anæmia (familial acholuric jaundice). The [illegible]

[illegible] the patient is "more jaundiced than ill". Many authorities believe that splenectomy should be advised in every case when the diagnosis is made, because of the occurrence of serious complications in a high percentage of cases at some later period in the disease The principal complications which may endanger life and greatly enhance the risk of operation are cholelithiasis and cholecystitis, and severe hæmolytic crises. On the other hand, since the familial form of the disease has been recorded in successive generations in people who were able to carry on their occupations with little or no ill-health, other authorities do not consider that splenectomy is indicated in the milder cases of this group Our own feeling is that, since it is impossible to foretell with certainty the future of even the mildest case of acholuric jaundice, it is wiser to advise operation while the patient is in good health than to risk the serious complications already mentioned. We have no hesitation in offering this advice if the anæmia is in any way affecting the patient's physical and mental health and causing a loss of efficiency Additional reasons for advocating splenectomy are a past history of hæmolytic crises or a history of the disease occurring in a severe form in relatives, since it has been shown that the course of the disease runs fairly true to type in different members of the same family. Splenectomy should also [illegible]

[illegible] complications are remote, and provided health is not impaired by anæmia, splenectomy may be safely postponed until the child is ten or twelve years of age, when the procedure is attended by less risk

Should acute inflammation of the gall-bladder, necessitating laparotomy, occur in a patient with acholuric jaundice, it is generally advisable to limit the operative procedure to the gall-bladder and to undertake splenectomy at a subsequent suitable date The interval between the operations should not, however, exceed a few months, since the excessive hæmolysis will continue until

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BLACKWATER FEVER AND POST-TRANSFUSIONAL HÆMOGLOBINURIA

(See pp. 199, 861.)

THE ACUTE HÆMOLYTIC ANÆMIA OF LEDERER

This may merely be a particularly acute form of hæmolytic anæmia, but it is sometimes considered as a separate entity. The presence of leucocytosis, high fever and anæmia has led many authorities to suggest that the hæmolytic process is due to an unknown infective agent, a view with which we are unable to agree, since identical manifestations are found in any severe hæmolytic anæmia.

The treatment to be adopted is blood transfusion, which should be repeated if recovery does not rapidly occur. Beneficial effects may result from blood transfusion in any type of hæmolytic anæmia, but the improvement which occurs in Lederer's anæmia appears to be much more rapid in onset and more lasting than in other hæmolytic anæmias Indeed, it is mainly this characteristic which has been responsible for the description of Lederer's anæmia as a separate entity.

If the hæmolytic process is not rapidly controlled by blood transfusion, the measures used for the treatment of idiopathic acquired hæmolytic anæmia (see p. 426) should be instituted

APLASTIC AND HYPOPLASTIC ANÆMIA

Aplastic and hypoplastic anæmias result from a loss, complete or partial, of the cells in the bone marrow that form erythrocytes, leucocytes and platelets

In certain cases, especially when the disease occurs in an acute form in young persons, the cause is unknown and the name "idiopathic or primary aplastic anæmia" is used, while in others—the disease may occur at any age—it is usually more chronic and is frequently secondary to some recognizable infective or toxic element.

Accordingly, it is desirable to have a clear conception of the causes known to produce an aplastic or hypoplastic state of the bone marrow

CAUSES OF SECONDARY APLASTIC OR HYPOPLASTIC ANÆMIA

(1) *Physical Agents*

(*a*) The heavy metals: gold, mercury, silver, bismuth, arsenic, lead
(*b*) The benzol compounds benzol, trinitrotoluol, dinitrophenol, etc
(*c*) Poisonous gases carbon monoxide, methane, mustard gas, nitrous oxide
(*d*) Radio-active materials and X-rays, radium, radon gas, thorium.
(*e*) Drugs: chloramphenicol, mepacrine, urethane, nitrogen mustards.

(2) *Hazardous Occupations*

(*a*) Benzol rubber workers, dry-cleaners, tanners, varnish and paint workers, gilders, feather workers, milliners, printers and tinners are engaged in occupations in which benzol is used for its solvent properties
(*b*) Lead: painters, plumbers, etc
(*c*) Trinitrotoluol: munition workers.

For those patients who fail to respond adequately to splenectomy, an attempt should be made to bring the hæmolytic process under control by further hormone therapy. Should this fail, the prognosis is extremely serious.

Symptomatic Hæmolytic Anæmia.—Symptomatic hæmolytic anæmia may be found accompanying such conditions as Hodgkin's disease, syphilis, tuberculosis, reticulum-cell sarcoma, carcinomatosis, etc. The treatment is that of the primary condition, supplemented by blood transfusion. Should the

Paroxysmal Hæmoglobinuria.—Hæmoglobinuria results from an intravascular hæmolysis sufficient to raise the plasma hæmoglobin above the renal threshold Accordingly it may occur in any type of anæmia resulting from intravascular hæmolysis. The following types are usually accepted as distinct clinical entities.

*Cold Hæmoglobinuria —In this type rapid hæmolysis leading to hæmo*globinæmia and hæmoglobinuria occurs when the patient enters a warm atmosphere after having been exposed to cold. Syphilis is the principal ætiological *factor. The condition can be recognized by the Donath-Landsteiner test*

Prophylaxis, which should include avoidance of all forms of chilling, e g. washing the hands in cold water or drinking cold fluids, is an important part of the treatment.

When syphilis is the cause, thorough and prolonged antisyphilitic treatment

Usually no treatment is necessary, since it is a mild disease which
when adult life is reached.

pulmonary ventilation during sleep.

Treatment is unsatisfactory and is mainly symptomatic. Splenectomy is contra-indicated. Hæmolytic crises are best treated with transfusions of 250 to 500 ml. of red cells which have been carefully matched and washed free of plasma Severe reactions are liable to occur after the transfusion of whole blood.

Fabismus.—Fabismus is the name given to a hæmolytic anæmia accompanied by severe hæmoglobinuria which is essentially confined to southern Europe, particularly Italy and Sardinia It is believed to result from the ingestion of the bean *Vicia faba* or inhalation from the bean plants which are grown in abundance in the localities concerned

Prevention consists in avoidance of the bean. Symptomatic measures should be adopted for the hæmolytic anæmia when required

BLACKWATER FEVER AND POST-TRANSFUSIONAL HÆMOGLOBINURIA

(See pp 199, 861.)

THE ACUTE HÆMOLYTIC ANÆMIA OF LEDERER

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Du[illegible]

be giv[illegible]

should be instituted If anæmia results, iron therapy (see p 404) should be instituted. These measures are equally applicable to all types of hæmoglobinuria.

Hæmoglobinuria on Exertion.—This type occurs in young males and is probably analogous to postural albuminuria.

Usually no treatment is necessary, since it is a mild disease which disappears when adult life is reached

Nocturnal Hæmoglobinuria (Marchiafava-Micheli syndrome).—The ætiology is obscure although it has been suggested that it is due to an inherent defect of the red cell which renders it susceptible to lysis when a slight lowering of the hydrogen-ion concentration of the blood occurs consequent on reduced pulmonary ventilation during sleep

Treatment is unsatisfactory and is mainly symptomatic. Splenectomy is contra-indicated. Hæmolytic crises are best treated with transfusions of 250 to 500 ml. of red cells which have been carefully matched and washed free of plasma. Severe reactions are liable to occur after the transfusion of whole blood.

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congestion and is identical with the pathological features found in the spleen in cases of primary cirrhosis of the liver, and hence is in keeping with the

obstruction to the flow of blood in the portal or splenic veins.

3. The absence of pathological changes in the liver in many cases of splenic anæmia can be explained by the block in the portal circulation being extra-hepatic in situation

4. Cirrhosis of the liver may progress and hæmorrhages from the stomach and œsophagus recur, or even start for the first time, subsequent to removal of the spleen

Accordingly, we are unable to agree that there is any satisfactory evidence in favour of the hypothesis that the disease starts primarily in the spleen and suggest that the consensus of modern opinion supports the view that the splenomegaly is secondary to portal hypertension.

reasons we feel that the names splenic anæmia and Banti's disease should be discarded and replaced by the term "the syndrome of portal hypertension" to describe the clinical and hæmatological features which result from an intra- or extra-hepatic block in the portal circulation.

Treatment will be considered under two headings:

1 Operative measures, including splenectomy.
2. Symptomatic treatment
   (a) Diet and iron.
   (b) Blood transfusion

Operative Measures.—The beneficial effects claimed for splenectomy

of surgery in the treatment of portal hypertension, the types of operation advised and the results achieved

the advisability of surgical treatment
ostruction to the
-hepatic in site.

Cirrhosis of the liver, especially of the Lænnec type, is the principal cause of intrahepatic obstruction Thrombosis of the portal vein or splenic vein due to inflammation trauma or pressure from without is the main cause of extra-hepatic obst
little or no
reducing th
intestinal bleeding The clinical history and physical
with the assessment of liver function by special tests and by biopsy, play an essential part in deciding on the advisability of operation and the most suitable surgical procedure. If advanced liver cirrhosis is present and the patient's clinical state is poor, surgical intervention is contra-indicated. If the assessment of the case indicates that pathological changes in the liver are only moderate,

slight or absent, while the dangers of hæmorrhage from œsophagea varices are great, operation should be undertaken. The details are c the findings after the abdomen has been entered. If the portal hyper due to intrahepatic block or to extrahepatic block in the portal vein, spl alone will fail to relieve the portal hypertension It was because of th ledge that operations were devised to shunt the portal blood into the circulation This can be accomplished by anastomosing the splenic ve left renal vein or the portal vein to the inferior vena cava Several yea elapse before a final assessment of the value of these procedures can b but already doubt is being expressed about the technical success of the op in relieving portal hypertension Hence it has been suggested that in s cases resection of the lower end of the œsophagus and the upper portion stomach may be the best means of preventing death from bleeding from in these situations When the block is extrahepatic and in the splenic splenectomy alone will cure the syndrome and remove the danger of hæmorr since only the splenic circulation is involved Splenic vein obstruction is less common than obstruction of the portal vein

Although splenectomy alone may not be able to influence materially mechanical factors which lead to bleeding in intrahepatic block and ex hepatic block in the portal vein, it may be of value in reducing the tendenc bleed if the platelets are markedly reduced, as is not uncommonly the c The presence of severe neutropenia and thrombocytopenia due to hyp splenism would accordingly be an additional reason for splenectomy in syndrome of portal hypertension Other operative procedures which have be undertaken with the object of reducing the incidence of hæmatemesis a ligation of the coronary vein of the stomach, ligation of the splenic artery and t production of a collateral circulation in the abdomen through post-operativ adhesions (omentopexy, Talma-Morrison operation) The results achieve are uncertain and usually unsatisfactory Treatment aimed at thrombosin dilated œsophageal veins by injecting them through an œsophagoscope with sclerosing solutions such as are used in the treatment of varicose veins of the legs, has been undertaken in a limited number of cases. Our experience of this ingenious but potentially dangerous procedure does not lead us to recommend it.

Symptomatic Treatment.—The general treatment of the anæmia in splenic anæmia is on the lines indicated on p 403 When a large hæmatemesis occurs, the patient suffers from acute post-hæmorrhagic anæmia, for the treatment of which see p 411 In other cases a chronic hypochromic anæmia results from continuous occult bleeding from the gastric and œsophageal varices, and the measures outlined on p 404 will be found to be suitable

Diet.—Articles of food which are liable to injure mechanically the gastric and œsophageal varices should be excluded from the diet or their irritating components removed The following articles should be excluded—highly seasoned and indigestible foods, condiments and pickles, the skins and pips of fruits, nuts, etc.—and coarse vegetables and fruits should be passed through a sieve and served as purées or fools When cirrhosis of the liver is present, a diet low in sodium is indicated (see p 524)

Iron—A study of the best-known textbooks of medicine suggests that iron is of little or no value in the treatment of the anæmia found in portal hypertension. Our experience of the excellent results which may frequently be obtained leads us to protest against this view We have obtained rapid rises in

the hæmoglobin level when iron was given in the preparations and doses stated on p. 404. The response to iron therapy is disappointing only in the late stages of the disease, when hepatic failure is imminent.

Blood Transfusion is of great value in the treatment of the shock following the severe hæmorrhages which occur in splenic anæmia. By this means we have repeatedly tided patients over emergencies and prolonged life for years. Iron therapy should be started immediately after the transfusion. Blood transfusions should be discontinued only when there is clear evidence that an advanced stage of liver failure has been reached or when hæmorrhages are recurring at short intervals and operative procedures to relieve the portal hypertension cannot be undertaken At this stage of the disease the patient is living on a volcano and the mental misery entailed by the constant fear of another hæmatemesis is of such a degree that it makes it inadvisable to attempt to prolong life. Palliative treatment

1 hæmatemesis, see p. 507.

MYELOFIBROSIS

Myelofibrosis is a rare disease of unknown ætiology which invariably terminates fatally. It is characterized by extensive replacement of the marrow by fibrous tissue and bone, the simultaneous development of extramedullary hæmopoiesis in many sites, particularly the spleen, and the appearance in the peripheral blood of primitive white cells and red cells. Sternal puncture usually yields no marrow tissue and the diagnosis can only be established with certainty by marrow trephine.

In most cases treatment is entirely symptomatic. Iron should be given if a hypochromic anæmia develops. Blood transfusions will usually be required to maintain the hæmoglobin at a satisfactory level. The spleen is invariably enlarged, and because it is considered to be the main site of extramedullary blood formation, most authorities have stated that splenectomy is strongly contraindicated. It is now believed that removal of the spleen is justified when a symptomatic hæmolytic anæmia develops to a degree requiring correction by frequent blood transfusions, or when there is clear evidence that the remaining marrow tissue is being suppressed by hypersplenism. In addition, a small proportion of patients become severely disabled by gross enlargement of the spleen. In carefully selected patients splenectomy has been shown to result in an improvement of the anæmia, a reduction in the number of blood transfusions required and the relief of abdominal pain and discomfort

POLYCYTHÆMIA VERA

(*Erythræmia*; *Splenomegalic polycythæmia*, *Vaquez's disease*; *Osler's disease*)

A rare disease characterized by polycythæmia, increase in the viscosity and volume of blood, and by cyanosis and splenomegaly.

Before one can conclude that a high red-cell count indicates an absolute increase in circulating cells, one must exclude (*a*) local congestion, e g. Raynaud's disease, (*b*) diminution of plasma volume (relative polycythæmia), e g. after severe sweating, vomiting or diarrhœa. An absolute increase of red cells results from one of two causes. (1) a primary disease of the erythroblastic tissues,

analogous to the hyperplasia of the leucoblastic tissues in leukæmia—hence the name "erythræmia"; and (2) a compensatory hyperplasia of the erythron secondary to factors which lead to incomplete oxygenation of the blood. The "... " should be confined to the latter type of polycythæmia. ...is are chronic cardiac and pulmonary ... at high altitudes and the toxic effects ... phosphorus, aniline dyes, etc. A diagnosis of polycythæmia vera should ... ver be made till the more common conditions which cause erythrocytosis have been excluded In relative and in ... treatment is concerned entirely with the underlying ... ardiac disease

... manifestations of polycythæmia vera are ... od volume and increased blood viscosity, ... of these features by reducing the number ... For this purpose many different methods have been employed, most of which have proved ineffective Splenectomy is contra-indicated Benzol should not be used because of its excessively toxic and depressant effect on the bone marrow Arsenic in large doses was formerly employed, but has been replaced by the forms of treatment mentioned ... Because of

employed

The physician has the choice of three main methods of treatment (1) venesection; (2) irradiation with X-rays, or (3) radio-active phosphorus A combination of these methods may be used

Venesection—To be of any value a large quantity of blood must be withdrawn, since the blood volume is often increased two- or three-fold Little relief is likely to follow the withdrawal of less than 1 litre (35 oz). There can be no ... more rapid relief from subjective symptoms than ...

...ely

Owing to the greatly increased viscosity of ... to be successfully accomplished unless certain modifications of the usual methods are employed

1. A wide-bore needle should be used, and the rubber connection attached to this and leading to the receptacle for the blood should be as short as is consistent with convenience and thoroughly washed with sodium citrate solution before use.

2. When the vein has been selected, the needle should be inserted in the ... ined in the blood receptacle to ... ng, and so prevent clotting.

... the sole method of treatment are that the effect is transitory, that even frequently repeated venesections may not achieve the necessary reduction in cell mass or may produce hæmoglobin deficiency without materially reducing the number of red cells, and finally,

that venesections do not produce any substantial reduction in the high platelet levels and consequent incidence of thrombosis.

Irradiation.—X-ray therapy is widely used in the treatment of polycythæmia vera, and the method generally recommended at present is that of irradiation of the whole of the patient's body, i.e. the wide-field or "bath" treatment (see p. 457). This method is preferable to older methods such as the localized irradiation of long bones in rotation. An interval of some weeks may elapse before the red-cell count begins to fall, and treatment should be terminated long before that event. If too much irradiation is employed, there is considerable danger of causing aplastic anæmia. Overdosage may result in irreparable damage to the bone marrow, while underdosage can always be corrected by employing a further course of treatment.

Radioactive Phosphorus P^{32} has been widely used in recent years for the treatment of polycythæmia vera, especially in North America. It is particularly suitable for therapeutic purposes because it has a short half-life of fourteen days and emits only the relatively innocuous beta particles Since phosphorus is deposited in bone, its radio-active isotope exerts its biological effect particularly on the actively proliferating cells of the bone marrow. For this reason its chief therapeutic value is in the treatment of certain blood diseases, especially polycythæmia vera and to a lesser extent chronic leukæmia. Compared with X-ray therapy it appears to be at least equally effective in producing and maintaining remissions, and no more prone to cause complications. It is, moreover, more convenient to administer, the isotope being injected intravenously or given orally as a solution of sodium acid phosphate. Because of the ease with which it can be given, the convenience to the patient and the absence of irradiation sickness, it is widely accepted at the present time as the treatment of choice. The usual initial dose either by mouth or injection is about 6 millicuries. No significant reduction in the blood count can be expected in less than four weeks If after three months the red-cell count is still greater than six million, a second dose, slightly smaller than the initial one, should be given. In most patients the ensuing remission will last at least one year and sometimes considerably longer.

Conclusions.—At the present time the method of choice in the treatment of polycythæmia would appear to be irradiation, either by wide-field X-ray therapy, or by radio-active phosphorus. Venesection should be employed in an emergency, in the initial stages of treatment by irradiation or as a supplement to the effects of irradiation

Symptomatic Treatment.—A patient with polycythæmia may complain of a variety of symptoms which are principally referable to the nervous, gastro-intestinal and cardiovascular systems. Since they are all due to the high blood volume and increased viscosity of the blood, the measures outlined above to [illegible] ...nt. [illegible] ...id [illegible] ...d (chloral hydrate and the barbiturates). For dyspepsia, a light easily digested diet together with alkalis is advised. Constipation should be treated as outlined on p. 499. Purging with salines should be avoided as this still further concentrates the blood.

The occurrence of hæmorrhage relieves the plethora and no treatment should be undertaken to stop it unless excessive quantities of blood are lost.

The liability to thrombosis is best reduced by controlled irradiation therapy and by prescribing regular exercise to maintain an active circulation.

ENTEROGENOUS CYANOSIS

(*Methæmoglobinæmia* ; *Sulphæmoglobinæmia*)

A disease characterized by chronic cyanosis due to the presence of methæmoglobin, or sulphæmoglobin, in the circulating blood

Prophylaxis.—In the great majority of cases the condition is caused by the ingestion of drugs, e g phenacetin, acetanilide, nitrites, sulphonal, potassium chlorate and trional; and recently much attention has been drawn to its frequent occurrence during the administration of the sulphonamide group The ...

... scopic examination of the blood The occurrence of sulphæmoglobinæmia may be prevented in a large proportion of cases by correcting constipation before prescribing any of the drugs mentioned During their administration regular bowel evacuations should be produced by liquid paraffin and occasional enemas rather than by laxatives or purgatives, in particular, saline purgatives should be avoided because they render the contents of the colon fluid and so increase the absorption of hydrogen sulphide.

Curative Treatment.—The alarming appearance of the patient is in striking contrast to the absence of any distress, and usually, no treatment is required other than withdrawal of the causative drug

If the concentration of methæmoglobin is high, symptoms due to anoxæmia may occur, particularly if the condition supervenes in a disease which by itself causes some degree of anoxæmia For example, methæmoglobinæmia may intensify considerably the anoxæmia in lobar pneumonia and in anæmia In ...

... injection into the subcutaneous tissue) and oral administration begun at the same time.

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C. *Defective Production or Excessive Destruction of Platelets*
(thrombocytopenic purpura)

1. Primary: idiopathic thrombocytopenic purpura.
2. Secondary: due to
   (*a*) Exposure to X-rays or radio-active substances
   (*b*) Severe infections which may damage the bone marrow in addition to the capillaries.
   (*c*) Drug intoxications, e g benzol, organic arsenicals, sedormid, gold, bismuth, mercury.
   (*d*) Blood diseases—aplastic anæmia, leukæmia and hypersplenism, as sometimes occur in Hodgkin's disease and the syndrome of portal hypertension, etc
   (*e*) Primary and secondary malignant disease of bones and bone marrow, myelomatosis, myelosclerosis and myelofibrosis
   (*f*) Diseases of doubtful ætiology, e.g acute lupus erythematosus, thrombotic thrombocytopenic purpura

In the hæmorrhagic diseases, in which the bleeding tendency may be caused [illegible]

[illegible]

occurs, to assess the degree of anæmia present and to establish whether the purpura is of the thrombocytopenic or non-thrombocytopenic variety. In conditions due to a defect in coagulation, the procedures needed to establish the precise nature of the deficient factor are complex, and the co-operation of a pathologist trained in these special techniques is essential

HÆMOPHILIA

Hæmophilia is a hereditary disease due to a deficiency of antihæmophilic globulin. It is characterized by a tendency to excessive hæmorrhage after slight trauma Males only are affected, while transmission of the disease is solely through females of hæmophilic stock The relative rarity of the disease and the spontaneous fluctuations in the tendency to bleed which occur make the merits [illegible]

[illegible]

activities and the type of work to be undertaken after school Conservative

sulphæmoglobinæmia is obtained and an increase in the hæmoglobin level is produced sufficient for the needs of the body. Methylene blue is ineffective in sulphæmoglobinæmia.

THE HÆMORRHAGIC DISEASES

The diseases included in this section are characterized by an increased tendency to bleed. In the purpuras, where there is damage to capillaries or a deficiency of blood platelets or both, hæmorrhages occur spontaneously in the skin (petechiæ, ecchymoses) and from mucous membranes, and there may be severe internal or external hæmorrhage. In the group of diseases due to a defect in the mechanism of coagulation, hæmorrhage is prolonged after slight trauma and may occur internally, for example into a joint, or externally after tooth extraction, cuts etc. The following classification is proposed as a useful working basis for the practitioner, but it must be understood that in some of the purpuras, that is in conditions listed under B and C below, capillary damage and thrombocytopenia may coexist.

A *Defects in the Clotting Mechanism*

1. Hæmophilia.
2. Christmas Disease
3. Hypoprothrombinæmia which occurs
   (*a*) in hæmorrhagic disease of the newborn;
   (*b*) in biliary obstruction and intestinal disorders such as sprue and ulcerative colitis;
   (*c*) in severe hepatic damage;
   (*d*) from anticoagulant drugs, e.g. of the coumarin type.
4. Fibrinogenopenia.

B. *Defects in, or Damage to, the Capillaries*
(Non-thrombocytopenic or vascular purpura)

1. Infections (usually severe in degree and particularly if a septicæmia is present) with *Streptococcus hæmolyticus* and *viridans*, meningococcus, *B. typhosus*, *B diphtheriæ*, *M. tuberculosis* (especially in miliary forms) and the Rickettsiæ of typhus fever and the viruses of measles, smallpox, etc.
2. Intoxication from, or idiosyncrasy to, drugs, e.g. sulphonamides, barbiturates, carbromal, quinine, aniline dyes, ergot, iodides.
3. Chronic diseases of kidneys and liver, malignant disease and, rarely, in the terminal stage of chronic cardiovascular disease.
4. Avitaminosis—scurvy
5. Allergic states, including Schonlein's and Henoch's purpura.
6. Congenital defects—hereditary telangiectasis; hereditary familial purpura (von Willebrand's disease).
7. Senile purpura.

hæmophilic factor temporarily to a safe level, a major operation, e g. for an abdominal emergency, is likely to result in fatal hæmorrhage.

Local Treatment.—When hæmorrhage occurs into a joint, the affected part

Deep-tissue hæmorrhage may have serious consequences as a result of pressure on nerves or blood vessels Again reliance must be placed on immobilization and correction of the clotting defect as described Incision or aspiration is never justified.

When the site of bleeding is accessible, much can be done to hasten hæmostasis and so to reduce the necessity for repeated transfusions of blood, plasma or AHG

one. Pressure at the site is often helpful when applied for a few minutes in

after extraction and the

is regarding the treat-

Dental Extraction.—Not more than two teeth should be removed at one time, and extraction should be preceded by the intravenous infusion of 2 pints (1 litre) of fresh plasma or the equivalent amount of AHG A general anæsthetic is to be preferred to local infiltration, which may lead to devitalization of the tissues and hæmorrhage. Great care should be taken during the extraction to reduce tissue damage to a minimum. The socket should then be lightly plugged with gauze or a soluble dressing (fibrin foam, oxidized cellulose or gelatin

blood becomes widespread and extends into the tongue and throat. As soon as respiratory embarrassment becomes evident, an anæsthetist's oral tube or a nasotracheal tube should be passed, and further transfusion of fresh blood or

soaked in coagulant solution. If the hæmorrhage is severe, a transfusion of 4 to 5 pints (2 3 to 2 8 litres) of fresh blood should also be given

dentistry (e.g. fillings and scaling) at frequent and regular intervals is of great importance. In this way the necessity for extraction of teeth at a later date is much reduced; (*c*) only essential operative procedures should be undertaken and they should be preceded by *careful measures to bring* about a temporary reduction of the tendency to bleed.

Treatment during an Attack of Bleeding.—*General Treatment.*—Recent work has established the following important principles:

(1) The bleeding tendency can be corrected temporarily only by the intravenous injection of fresh blood or plasma or a derivative of blood containing the antihæmophilic factor (usually called antihæmophilic globulin or AHG).

(2) Satisfactory treatment entails the use of much larger quantities of blood, plasma or AHG than was formerly realized. It is now known that a hæmophilic may start to bleed when the clotting time (Lee and White method) is normal, and he may continue to bleed when a prolonged clotting time is restored to normal by blood or plasma transfusion. It is believed that the antihæmophilic factor must be increased to at least 30 per cent. of normal before the bleeding tendency can be regarded as having been overcome. The clotting time may be normal with a much lower concentration of AHG than this, and only more elaborate procedures *like* the thromboplastin generation test may reveal the abnormality.

When hæmorrhage occurs in a hæmophilic, treatment should be instituted as soon as possible, because persistence of the hæmorrhage will lead to blood dilution and still further lowering of the concentration of AHG. The transfusion of 4 to 5 pints (2·3 to 2·8 litres) of fresh blood (removed not longer than three hours before use) or 2 pints (1 litre) of fresh plasma, or an equivalent

available in the near future. Human plasma which has been frozen solid or has been freeze-dried while still fresh retains its AHG potency for months. In centres with suitable facilities, a supply of this plasma specifically for use in hæmophilics would serve a useful purpose. Human serum is of no therapeutic value in hæmophilia.

It has been thought in the past that some patients may become refractory to blood, plasma or AHG transfusion as a result of antibody formation to the antihæmophilic factor. *Now it is believed that many examples of this so-called* refractory state have been due to the use of insufficient amounts. Moreover, when AHG used alone in adequate doses fails to correct the bleeding tendency it is possible that a wrong diagnosis has been made and the patient may not be suffering from hæmophilia but from Christmas disease

Treatment on these lines should be adopted in all cases where the site of bleeding is inaccessible, or where local measures have failed to control bleeding in accessible situations, e.g. teeth, nose, skin. It should immediately precede any surgical procedure such as tooth extraction. Major surgical operations should not be undertaken in hæmophilics until it is clear that the patient will die without this intervention. Even with energetic measures to restore the anti-

intravenously. The "prothrombin time" should be estimated four hours later and the injection should be repeated if it has not returned to a safe level. In less urgent cases 10 to 20 mg., i e 1 to 2 capsules, of Konakion should be given by mouth and the "prothrombin time" determined after eight hours. The same dose or a smaller one may then be given if the response has been inadequate It is seldom necessary to give more than two doses either intravenously or orally.

In obstructive jaundice, biliary fistula, prolonged diarrhœa and severe hepatic disease it is probable that the water-soluble vitamin K analogues are as effective as synthetic vitamin K_1, and, since they are cheaper and can be given in larger doses without untoward effects, they should be preferred. Synkavit (Roche Products) or Kapilon (Glaxo) can be given subcutaneously or intramuscularly in a daily dose of 10 to 20 mg (1 to 2 ampoules). In hypoprothrombinæmia due to obstructive jaundice, biliary fistula and prolonged diarrhœa the response is usually rapid and the prothrombin level is restored to normal in less than a week In hepatic disease the response is usually disappointing, since a severely damaged liver cannot utilize vitamin K adequately In such cases

ing has ceased Larger doses may cause hæmolysis in premature infants. Insufficient information is available about the effects of synthetic vitamin K_1 to justify its use in this form of hypoprothrombinæmia at present. Ascorbic acid, 50 mg. by mouth twice or thrice daily, may be given in addition, since there is some evidence that deficiency of vitamin C may be a contributory factor in some cases. Blood transfusion may be necessary if blood loss has been severe, and iron (see p 404) should be used in the treatment of the post-hæmorrhagic anæmia. At one time it was firmly believed that injections of a water-soluble vitamin K analogue to the mother during labour greatly reduced the incidence of hæmorrhagic disease in the baby, but more recently doubts have been expressed regarding the efficacy of this procedure In any event the injection of the infant is a more certain method of ensuring an adequate supply of vitamin K. Even when this is done, hæmorrhagic disease of the newborn may occur, and accordingly even this procedure is of doubtful prophylactic value.

FIBRINOGENOPENIA

Deficiency of fibrinogen may rarely occur as a hereditary defect, in which case the condition has to be distinguished from hæmophilia and Christmas disease

Examples of acquired deficiency are now recognized more frequently. In almost all cases the deficiency arises as a result of some abnormality during pregnancy, e.g accidental ante-partum hæmorrhage, abortion, intra-uterine death of the fœtus and amniotic embolism, but it can result from major thoracic surgery Blood transfusion is helpful in increasing the fibrinogen content of the blood and in correcting the effects of hæmorrhage, but very large volumes of

Christmas Disease

Usually the treatment is simpler than in hæmophilia because the bleeding tendency is less severe and it is probable that the transfusion of stored blood, plasma or serum is as efficient as fresh blood, since the activity of the Christmas factor is retained when blood is stored, in contrast to the destruction of anti-hæmophilic globulin *which occurs with storage. AHG is, of course, valueless* General measures and local treatment are the same as in the case of hæmophilia

HYPOPROTHROMBINÆMIA

the concentration of factor VII, it is convenient to retain it.

Low levels of prothrombin and factor VII, with resulting hæmorrhagic manifestations, may occur in the following circumstances:

(1) In prolonged obstructive jaundice and in chronic biliary fistula there is impaired absorption of the fat-soluble substance, vitamin K, which is essential for the formation of prothrombin and factor VII.

(2) Defective absorption of vitamin K may occur in diseases with prolonged and severe diarrhœa, such as sprue and ulcerative colitis.

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is thought that vitamin C deficiency may coexist in some cases.

Treatment.—A good deal of confusion has arisen regarding the precise meaning of the terms "vitamin K" and "vitamin K_1". Vitamin K occurs naturally in two forms, vitamin K_1 and K_2. Since vitamin K_2 is not important in medical practice, it need not be discussed further. Vitamin K_1 is 2-methyl-3-phytyl-1 · 4-naphthoquinone, and a synthetic preparation is now available in a water-miscible form in capsules each containing 10 mg. for oral use, and in ampoules containing 10 mg. for intravenous or intramuscular injection (*Konakion, Roche Products*). Accordingly it is no longer necessary to use vitamin K_1 dissolved in oil, since its intravenous use is contra-indicated; and when given orally in cases of obstructive jaundice and biliary fistula, bile salts have to be given simultaneously to ensure its absorption

The other substances which are frequently referred to as vitamin K are analogues having a similar action *in most*
The oil-soluble preparation, menaphthone,
muscular injection, is now obsolete. The
Synkavit (Roche Products) and Kapilon (Glaxo) are still very useful, since they are effective in some hypoprothrombinæmic states and they are relatively inexpensive.

In the hæmorrhagic state which may result from the use of the coumarin

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whole blood would be necessary to raise the fibrinogen content to a safe level. The *intravenous injection of 4 to 6 g of fibrinogen in solution is usually effective*, but fibrinogen preparations are in short supply in Britain although they can sometimes be obtained from Regional Transfusion Centres. A very efficient substitute is dried plasma, which is always available in well-equipped maternity units. One pint (0·56 litre) of reconstituted quadruple-strength freeze-dried plasma can be expected to
of this amount is rapidly
because it may lower the fibrinogen level.

While the above procedures will produce only a temporary alleviation of the bleeding tendency *when the fibrinogenopenia is hereditary, they lead to clinical* cure when the deficiency is acquired and self-limited.

THE PURPURAS

The purpuras are best divided into two groups:

- Primary or Idiopathic—in which no cause can be found.
- Secondary or Symptomatic—in which the symptom-complex is due to a recognizable cause.

purpuric spots not infrequently appear during the course of the exanthemata and occasionally in children without any obvious cause. In addition, senile purpura is confined to the skin and no treatment beyond protection from trauma is indicated. On the other hand, a mild degree of purpura may appear in the late stage of very serious diseases such as chronic nephritis and malignant disease *In such cases treatment is directed to the causative disease and no* particular treatment for the purpura itself is required.

In purpura of moderate or severe degree there may be persistent hæmorrhage from tooth sockets, from the nose and from other accessible sites. In these cases local treatment is valuable and the instructions given for the local control of hæmorrhage in hæmophilia *should be followed*

Idiopathic Thrombocytopenic Purpura

As the name implies, the disease is characterized by a reduction in the number of or less; *in addition*, the bleeding ti ased. Splenomegaly is rarely prese is unknown. Recent work suggests that it may be due to the presence of a circulating auto-agglutinin for platelets.

The main methods of treatment are (*a*) blood transfusion, (*b*) the *administration* of hormones, and (*c*) splenectomy.

Blood Transfusion.—The number of blood platelets can be increased only slightly and transitorily by transfusion of blood even when fresh. But blood transfusion i [illegible]
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and the indications for blood transfusion in acute post-hæmorrhagic anæmia are given on p 412. If blood loss is persistent or recurrent, transfusions will have to be repeated Apart from their use as an emergency measure in the treatment of acute severe hæmorrhage, blood transfusions are of particular value in the following circumstances.

(1) In children with persistent or recurrent hæmorrhage, blood transfusions can maintain the hæmoglobin at a reasonable level until spontaneous remission occurs—as it usually does in children.

(2) When splenectomy has become necessary, blood transfusion should be given to raise the hæmoglobin level to 80 per cent or more prior to the operation

Corticotrophin and Cortisone, Prednisone and Prednisolone.—As in the hæmolytic anæmias (see p 427), the precise role of these hormones in the treatment of the purpuras has not yet been defined It appears that in many [illegible]

The doses mentioned in the section on The Hæmolytic Anæmias (see p. 427) should be tried , in this way it is possible that the condition of the patient may be improved to a greater extent than by blood transfusions alone and so splenectomy may be accomplished with less risk If hormone therapy appears to induce a complete or near-complete remission, splenectomy may justifiably be postponed and the patient should be observed carefully for signs of relapse after withdrawal of the hormone If these appear, splenectomy is the treatment of choice preceded, if necessary, by blood transfusion and perhaps another course of hormone therapy. In patients who relapse after withdrawal of the hormone and in whom a contra-indication to the major operation of splenectomy exists, continuation of hormone therapy for an indefinite period is justified. Similar therapy may be indicated in patients who relapse after splenectomy.

Splenectomy is indicated as an emergency measure in patients who have persistent severe hæmorrhage leading to dangerous anæmia and shock, despite massive blood transfusions [illegible]
situation, e g. the brain T [illegible]
followed by further blood [illegible]
pre-operative measure is dc [illegible]
splenectomy are high, the mortality varying from 10 to 30 per cent. in different hands, but the risks from the hæmorrhagic state in these intractable cases [illegible]

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Hodgkin's disease with marked constitutional features of fever and loss of weight and appetite, and when the mediastinal and abdominal glands are affected. Remarkable improvement may be produced in such cases by repeated courses of treatment at adequate intervals. For details of dosage and technique of administration, see p. 460. Cortisone and corticotrophin are occasionally of value in ameliorating the constitutional features and in reducing the size of the glands, especially if they are causing pressure symptoms, but the remissions produced are usually short in duration and not so satisfactory as those obtained with X-ray therapy or nitrogen mustard. On theoretical grounds it might be suggested that if the disease affects an isolated group of glands and is of low malignancy, surgical removal should be undertaken. In practice this is seldom done, because the results are no better than those obtained from localized X-ray therapy. Splenectomy should be recommended only if there is clear evidence of *hypersplenism or symptomatic hæmolytic anæmia.*

In some cases arsenic is employed between the courses of X-ray therapy according to the method described on p. 458 Iron (see p. 404) should be

troublesome symptom.

The general measures which should be adopted are the same as for the leukæmias (see below).

MULTIPLE MYELOMA

Multiple myeloma is a rare disease of unknown ætiology mainly affecting people over the age of forty and involving the skeleton in widespread changes. The condition is probably a malignant disease of the plasma cells, i.e. a plasma cell sarcoma. The prognosis is bad, death occurring usually within two to three years.

There is no curative treatment, but symptomatic relief and healing of the

thus permitting the recalcification of bone. If the systemic effects of the disease are absent, e g. bone pains, anæmia, fever, loss of weight and strength, no

chemotherapy at

well-being

r, *systemic*

features of ill-health are present, treatment with urethane given orally or with

Recently

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e pp. 463,

kala-azar,

464) Stilbamidine, an antimony compound

was introduced in 1948 as a remedy for multiple myeloma in which, as in *kala-azar*, the serum globulin is high. The hopes raised at that time have not been

has been largely abandoned.

for the treatment

matosis.

DISEASES OF LIPOID METABOLISM

Gaucher's disease
Niemann-Pick disease
Hand-Schuller-Christian disease

It has been customary in the past to include Hand-Schüller-Christian disease in this group of rare disorders, but recent evidence suggests that it ... granuloma. There is no ... pochromic anæmia ... Some authorities recommend splenectomy in all cases in which ... osis of Gaucher's disease has been established, because of the great discomfort caused by the ... splenic mass in the late stages of this disease. In our opinion the ... more rapidly after ...

... level is found it may be reduced by a diet low in fat, and ... the progress of the disease X-ray therapy is of no value in Gaucher's disease or in Niemann-Pick disease, but will cause a disappearance of the tumours and of the osteolytic areas in the bones in the Hand-Schuller-Christian syndrome. Although the general health may be little improved, the liability to spontaneous fractures is reduced and pressure symptoms are ameliorated In this disease there may be obvious pituitary dysfunction resulting in diabetes insipidus and retarded growth, etc (see pp 375, 376)

THE LEUKÆMIAS

... diagnosis is made by examining a thin prepared ... bone marrow which will show the presence of a high proportion of stem cells which may be lymphoblasts, myeloblasts or monoblasts In the chronic leukæmias, on the other hand, the total white-cell count is usually greatly ... cells form only ...

... acute ... nths, despite recent advances in chemotherapy and hormone ... e the course of the chronic forms extends over a period of years Lymphatic leukæmia must be distinguished from glandular fever and acute infectious lymphocytosis, and sub-leukæmic and aleukæmic leukæmia from aplastic anæmia, agranulocytosis and myelofibrosis.

CHRONIC LEUKÆMIAS

... forms

General Measures

The average expectation of life in the chronic leukæmias has been found to be about three to five years The duration may be considerably longer in chronic lymphatic leukæmia in middle-aged and elderly persons. In fact, the expectation of life in such cases may be little affected by the disease, a point to be remembered when ordering potentially dangerous forms of treatment. In such cases no therapy is often the best therapy. Specific therapy with X-rays or drugs should be advised when definite symptoms appear and signs of activity of the disease are present, such as loss of weight and appetite, fever, anæmia, pressure features, etc., and not merely because of the diagnosis of chronic leukæmia. Because of the relatively long duration of the chronic leukæmias, the physician's attitude to patient and relatives should be both helpful and encouraging. No matter what form of treatment is employed, a fatal termination invariably occurs in all types of leukæmia. Nevertheless, radiotherapy or chemotherapy can increase the period of economic efficiency and comfort and possibly prolong life for a few months. Accordingly the patient should be advised to continue at his occupation or routine duties for as long as possible. Common-sense measures should be adopted regarding the regulation of the patient's life in regard to over-work, excessive exertion and chilling. Infections produce a marked deterioration in the health of patients with leukæmia. Hence, such patients should avoid close contact with persons suffering from colds in the head, sore throats, influenza, etc , and places where persons are crowded together during epidemics. Should a patient with leukæmia contract even a mild infection, he should receive medical supervision and remain in bed until the condition has completely cleared up

Careful instructions should be given to the patient that while exercise in the fresh air, such as walking, golfing and bicycling, is of value in maintaining health the amount undertaken should always be well within the limit of his tolerance. An ordinary mixed diet should be advised and the total calories should be high in view of the increased basal metabolic rate so frequently present in leukæmia This can easily be attained by prescribing additional quantities of butter, cream, bacon and the foods rich in carbohydrate.

Eventually, despite all treatment, emaciation and anæmia develop and the patient will have to give up his occupation and spend more and more time in bed. It is at this stage that blood transfusion is of value in improving the patient's general health and thus allowing the continuation of irradiation therapy.

In the terminal stages, when anæmia is severe and hæmorrhage and sepsis are occurring locally in the nose, mouth, etc., large and increasing doses of morphine are indicated.

Specific Measures

Specific treatment is aimed at reducing the proliferation of leukæmic tissue in the bone marrow, liver, spleen and lymph nodes, whilst permitting these organs to continue their normal function. This may be achieved in a variety of ways, but the presently available therapeutic measures have no more than a temporary effect. It should be realized that irradiation and chemotherapy exert their action on normal as well as abnormal cells , thus the difference between the effective and toxic dose is often very small. Much research has been devoted

to the development of substances with a wider margin of safety, but so far no agent with an action directed solely against the malignant cell has been found.

Irradiation Treatment.—(*a*) *X-ray Therapy.*—Since its first use in chronic leukæmia in 1908, X-ray therapy has stood the test of time; it is the standard by which the effectiveness of more recent agents is measured. Although some of the newer chemotherapeutic substances promise well, they have not been used for a long enough period to permit satisfactory statistical appraisal of their value compared with each other or with X-ray therapy. Until chemotherapeutic agents are shown to be superior to the latter, X-ray therapy should remain the treatment of choice.

The patient should be in hospital for the first course of irradiation, but if for some reason this is impracticable, he may be treated as an out-patient under

will be found a discussion on X-ray therapy.

cation to the use of X-rays. On the con-

crowding out of erythroblastic tissue by leucoblastic tissue, properly controlled irradiation is generally followed by a rise in hæmoglobin and circulating erythrocytes Transfusion of blood may be employed in anæmic individuals undergoing irradiation therapy in order to tide them over the period which must elapse before regeneration of red-cell marrow can occur

A time will come when destruction of erythroblastic tissue occurs, with the production of anæmia which cannot be controlled by iron or blood transfusion. When this stage has been reached, active treatment should be stopped and morphine or other symptomatic measures used to keep the patient comfortable.

(*b*) *Radio-active Phosphorus*.—The results reported in chronic leukæmia appeared to be similar to, but no better than, those expected from X-ray therapy. The dangers are even greater, and accordingly we do not recommend its use in leukæmia.

Drug Treatment.—*When skilled X-ray therapy is not available or where it has not been successful, treatment with chemotherapeutic agents or hormones should be instituted* These can be expected to induce in a considerable proportion of patients remissions of varying degree and duration. The chemotherapeutic agents may be classified in two groups.

1. Those with a specific nuclear toxic effect in arresting mitosis, as in the case of nitrogen mustards, myleran, urethane and colcemid
2. Those which act as metabolic antagonists to substances essential for cell growth, e g. aminopterin, amethopterin and 6-mercaptopurine.

all such drugs are capable of producing severe

safer and more

the choice of drug to be employed in the treatment of the

have recently been synthesized and

controlled clinical trials. We believe that the chemotherapeutic agents of value in the treatment of chronic myeloid leukæmia, in order of merit, are

Myleran, colcemid and 6-mercaptopurine, the nitrogen mustards and urethane. 6-mercaptopurine has the additional advantage that it may favourably influence the acute myeloblastic state which so often supervenes in chronic myeloid leukæmia. *For chronic lymphatic leukæmia* we suggest the oral nitrogen mustard derivative triethylene melamine (TEM). American authorities claim a 60 per cent. remission rate from the use of the drug. The course of chronic lymphatic leukæmia is not influenced by myleran, colcemid or 6-mercaptopurine. For details of dosage and methods of administration of the chemotherapeutic agents mentioned above, see p. 464.

Brief notes are also required on arsenic and on adjuvant measures sometimes employed, such as iron, cyanocobalamin, liver extracts and folic acid.

chemotherapeutic agents mentioned above, its use can no longer be recommended.

Iron.—If an iron-deficiency anæmia is present in chronic leukæmia, it requires treatment with dietetic treatment and medicinal iron, as described on p. 403.

Cyanocobalamin, Liver Extract, Folic Acid.—A macrocytic anæmia is sometimes seen in cases of leukæmia due to excessive activity in the remaining portions of erythroblastic marrow. As it is not associated with a deficiency of cyanocobalamin or folic acid, no benefit can be expected from administering these agents. There is in fact some evidence to suggest that folic acid and folinic acid may accelerate the leukæmic process.

Splenectomy is worthy of consideration in the chronic leukæmias if a symptomatic hæmolytic element can be shown to be the principal cause of the anæmia and if hormone therapy has failed to control the process.

ACUTE LEUKÆMIAS

Owing to the similarity in the hæmatological picture and clinical course it is convenient to consider all forms of acute leukæmia together. Acute lymphatic (lymphoblastic) leukæmia is the most common type encountered and occurs with especial frequency in children, often in the subleukæmic and aleukæmic forms. Acute myelocytic (myeloblastic) leukæmia and acute monocytic leukæmia occur at all ages. The prognosis is so uniformly bad no matter what form of

it is justifiable to

cases a remission

months, thus adding to the anguish of relatives when the fatal outcome inevitably ensues. Furthermore, these drugs are not only uncertain in their action but cause extremely dangerous and unpleasant side-effects. Nevertheless, we feel that chemotherapy should be advised for three reasons. First, most relatives wish

few extra weeks or months of life

sks involved and that death is

ician hope that the remission

nd that during

Lastly, it is

notherapeutic

agents can be assessed. Accordingly, we recommend that after the situation

has been clearly explained to the relatives it is both morally right and scientifically desirable to employ such treatment in all cases of acute leukæmia.

There are three groups of agents that can be used: hormones (corticotrophin, cortisone, prednisone and prednisolone), folic acid antagonists (aminopterin and amethopterin) and purine antagonists (6-mercaptopurine) The choice of drug depends upon the predominant cell type and the age of the patient. Thus folic acid antagonists have no value in acute leukæmia of adults, and monocytic leukæmia is influenced only by 6-mercaptopurine. Apart from these exceptions, all three groups of drugs will produce partial or complete remissions in about 50 per cent. of cases. Children with acute leukæmia are much more likely to benefit from chemotherapy or hormones than adults, and

COMBINED TABLE OF RESULTS IN THE TREATMENT OF ACUTE LEUKÆMIA

	Children			*Adults*		
	Total No of cases	*Remissions*	*Failures*	*Total No of cases*	*Remissions*	*Failures*
ACTH and Cortisone	175	80 (45%)	95 (55%)	46	14 (32%)	32 (68%)
Folic acid Antagonists (Aminopterin or Amethopterin)	460	234 (51%) Complete 126 (28%) Partial 108 (23%)	226 (49%)	68	6 (10%) Complete 4 (7%) Partial 2 (3%)	62 (90%)
Purine Antagonists (6-Mercaptopurine)	324	195 (60%) Complete 114 (35%) Partial 81 (25%)	129 (40%)	204	81 (40%) Complete 24 (12%) Partial 57 (28%)	123 (60%)

2nd Clinical Conference on ACTH, December 1950, Chicago.
2nd Conference on Folic Acid Antagonists, 1951, Boston
Conference on 6-Mercaptopurine, 1954, New York

lymphoblastic leukæmia is more susceptible to treatment than myeloblastic or acute monocytic leukæmia.

Most authorities in Great Britain believe that cortisone, prednisone or prednisolone therapy is the treatment of choice and that chemotherapy should not be given until it is clear that no response to hormone treatment is going to take place or until the inevitable relapse has occurred Other authorities, especially in North America, hold that hormone therapy and [illegible]

pressure effects of enlarged lymph nodes, since beneficial results may be expected within two to ten days as compared with two to four weeks with chemotherapy. When hormone therapy has been started, it should be continued until resistance develops, when chemotherapy should be commenced. In most other cases we believe that 6-mercaptopurine is the drug of choice, not only

because it may be effective in all types of leukæmia but also because the incidence and duration of remissions is greater than with hormone therapy, while the undesirable side-effects are less than those resulting from the folic acid antagonists.

When the leukæmic process becomes resistant to 6-mercaptopurine, as it invariably does, hormone therapy should be used. The folic acid antagonists may be of value when the disease has become resistant to both 6-mercaptopurine and hormones. Some authorities believe that the best results are obtained when these agents are used intermittently, administration being discontinued during remissions, while others hold that continuous maintenance treatment is indicated. We favour this latter view.

For details of dosage and methods of administration of cortisone, prednisone and prednisolone, see p. 85, of 6-mercaptopurine, see p 467; and of amethopterin and aminopterin, see p 465. The danger of producing aplastic anæmia and other serious toxic effects is so great with these antimetabolic drugs that they should be used only by physicians with a special knowledge of the problems involved.

X-ray therapy cannot be recommended, since it does not influence the course of acute leukæmia beneficially and may actually be harmful

Blood transfusions are often required to counteract the progressive anæmia. A concentrated preparation of washed red cells may be preferable to whole blood, as it leads to fewer undesirable reactions and reduces the risk of overloading the circulation "Exchange" blood transfusions as a form of specific treatment for acute leukæmia are not recommended because of the technical *difficulties involved and their failure to produce remissions sufficiently frequently* and of adequate degree to warrant the potential risks. Hæmorrhage from the nose and gums and other accessible sites should be controlled by the measures described on p. 441. Internal hæmorrhage not controlled by blood transfusions should be treated by the transfusion of viable platelets Platelets can be preserved by coating all transfusion apparatus (including the "taking" set) with silicone, or by the use of plastic blood containers and tubing, a method widely employed in North America.

Antibiotics are often necessary to control the infections acquired by patients with leukæmia, but intramuscular injections should be avoided because of the danger of producing large, painful and infected hæmatomas.

ALEUKÆMIC (SUBLEUKÆMIC) LEUKÆMIA

Aleukaemic leukæmia may be defined as a leukæmia *in which the abnormal* white cells are found to infiltrate the bone marrow and many organs of the body although the white-cell count is low or within normal limits. The differential count may be *qualitatively normal or abnormal* Diagnosis obviously presents the greatest difficul [illegible] the bone marrow, obtained by biopsy, is [illegible] ay occur in the acute form, clinically [illegible] te [illegible] treatment is on the lines already [illegible] whether [illegible] bnormal cells to enter the peripheral blood makes assessment of dosage extremely difficult. The risks of producing aplastic anæmia are so serious that some authorities

hold that both forms of treatment are contra-indicated. We feel, however,

therapy should be advised. Obviously, treatment must be given tentatively in small graduated doses, using the erythrocyte and platelet counts and the clinical state of the patient to assess its efficacy.

The other measures found to be of value in the frank leukæmias should also be used in aleukæmic leukæmia

X-RAY TREATMENT OF POLYCYTHÆMIA VERA, LEUKÆMIA AND THE RETICULOSES

In the treatment of the above diseases X-ray therapy is the method of choice and the use of radium has been abandoned. Daily treatment in small doses is preferable to weekly or monthly treatments with large doses. In polycythæmia vera and in the generalized types of reticulosis it is now customary to irradiate the whole of the patient's body In this so-called wide field or "bath" treatment, the dosage employed is a mere fraction of what is required when localized treatment is given to each area of involvement in turn Moreover, the patient is usually less upset by wide-field treatment and the benefit

of sterilization. In chronic leukæmia irradiation of the spleen has in the past been the method most generally used A satisfactory fall in the white-cell count occurs and patients have been maintained in good health for several

hæmatological results as good as those obtained by the local irradiation of the spleen, together with the additional benefits mentioned above. The wide-field method is probably the method of choice Localized treatment may still be given in certain types of the reticuloses where the disease is confined to a limited group of glands.

When X-ray treatment is given, the dosage must be carefully controlled by means of repeated clinical examinations and frequent blood counts, which, in addition to white-cell counts, should include examination of the erythrocytes, hæmoglobin and platelets.

Polycythæmia Vera.—The immediate effects of treatment may not be obvious, since several weeks may elapse before the red-cell count begins to fall. It is important therefore that treatment should terminate before there is any marked reduction in the red-cell count If treatment is carried on too long, there is a danger of producing aplastic anæmia. It is better to give too little than too much, because the course of treatment can always be repeated if too little has been given.

Chronic Leukæmia.—In leukæmia, treatment should be continued until the white cells fall to about 20,000 cells per c.mm. The rate of fall, however, is the most important guide to treatment If the white cells fall rapidly, then

treatment should be stopped before the above figure is reached. If they fall slowly, irradiation may be continued even after the count has reached 20,000 As mentioned above, it is most important that full blood counts should be made. In a case successfully treated, the red cells and hæmoglobin rise as the white-cell count falls and the patient's general health improves When a fall in red cells and hæmoglobin coincides with a fall in the white-cell count, the patient is unlikely to benefit to the same extent. In these circumstances blood transfusion may be of real value in helping to sustain the patient while awaiting the improvement in erythropoiesis

The Reticuloses—In the localized reticuloses, in addition to regional irradiation it is advisable to treat the adjacent lymphatic areas, even though they are not manifestly involved. This procedure seems to slow down the rate of advance of the condition. In fact, in localized reticulum-cell sarcoma irradiation may sometimes lead to complete eradication of the disease It is doubtful if such success ever results from the treatment of localized lymphadenoma or lymphosarcoma

When the reticuloses become widespread, "bath" treatments may be employed, though as a rule by this time the disease has reached a stage when it is doubtful if irradiation materially affects the duration of life. The aim is to improve the patient's general health It is important that this objective should be kept in view, and it is better to have a fit patient with some enlarged glands than an *ill patient with a complete regression of glandular enlargement. As in* chronic leukæmia, X-ray therapy should be reserved for the treatment of

[illegible] completion of the course of [illegible] should be made at intervals of two to three months Further treatment is indicated by deterioration of the patient's general health, and in the case of leukæmias and reticuloses it is more important to be guided by this rather than by the white-cell count or by the degree of glandular enlargement. The hæmoglobin level and the red-cell and platelet counts are of great value in immediate prognosis. Eventually a stage will be reached when further treatment results in no improvement in the *patient's well-being or in the concomitant anæmia.* In such cases, especially if purpura is present, treatment should be stopped irrespective of the blood count or of the size of the glands

X-ray Sickness.—The symptoms of malaise and vomiting which may develop during irradiation therapy are, as a rule, not marked unless large areas of the body are being irradiated. Adequate screening of the parts not *requiring irradiation and careful control of the daily dosage do much to minimize* these effects Many drugs have been tried both in the prevention and in the treatment of X-ray sickness, but none has proved entirely successful Sedative drugs such as phenobarbitone 60 mg (1 gr.) or chlorpromazine 25 mg or hyoscine hydrobromide 0 3 mg. ($\frac{1}{200}$ gr.), three times a day, are probably the most effective.

STANLEY DAVIDSON.
H W. FULLERTON.

CHEMOTHERAPY IN MALIGNANT AND ALLIED DISEASES

WITHIN THE MODERN ERA perhaps the best known of the earlier attempts to treat malignant and allied diseases with chemical substances was the use of arsenic in leukæmia, of which Forkner was a leading advocate, and of lead in cancer, as extolled by Blair Bell. The claims made by Coley for certain bacterial toxins in the treatment of sarcomata will also be recollected by older readers Although these substances have fallen into disuse, they have been replaced, during the past ten years or so, by a considerable number of other agents which have been credited with varying degrees of therapeutic efficacy Many of these agents reflect fundamental advances that are being made in the attack on the problem of malignant disease, and as such command wide interest It must be admitted, however, that the

expert supervision.[1] For this reason it is felt that a useful purpose may be served by taking stock of the present position, and indicating the possibilities and limitations of some of the chemotherapeutic substances which have recently

essentially an empirical one and is based upon the results of experience rather than upon theoretical principles It is limited to drugs which are generally available in hospital practice in this country.

CHEMOTHERAPEUTIC AGENTS AND THE PATHOLOGICAL CONDITIONS IN WHICH THEY MAY BE EFFECTIVE

Agent	*Diseases*
Nitrogen mustards and Triethylene melamine (TEM)	Hodgkin's disease and other reticuloses, chronic leukæmias; polycythæmia vera; bronchogenic carcinoma.
Urethane	Chronic myeloid leukæmia, multiple myelomatosis.
Myleran	Chronic myeloid leukæmia
Colcemid	Chronic myeloid leukæmia
Aminopterin and Amethopterin	Acute leukæmias.
6-Mercaptopurine	Acute leukæmias, chronic myeloid leukæmia, monocytic leukæmia.

essential that none of it be allowed to escape into the tissues. For these reasons it is recommended that the solution be injected into the rubber tubing of a freely flowing saline infusion previously set up for this purpose. By this method the risk of leakage into the tissues is minimized It is essential, however, to ensure that the needle is entirely within the vein and that the saline is flowing without leakage before injecting the nitrogen mustard.

The usual daily dosage is 0 1 to 0·15 mg. per kg. of body-weight, and a single

Daily injections during four consecutive days constitute the initial course of treatment most frequently adopted Other authorities administer the drug every three or four days and in the intervals assess the toxic effects by the clinical results and the white-cell count before giving the next injection. Such a course may be repeated when the patient relapses. In many cases, however, it may be preferable to follow up the initial course by a dose at weekly intervals until the patient appears to be in a state of satisfactory remission, or until it is evident that he is deriving no benefit This procedure is particularly suitable when it is desired to combine nitrogen mustard with X-ray therapy. It is not usually feasible or desirable to continue these weekly doses for more than five or six weeks continuously, and in view of the powerful depressant action of nitrogen mustard upon the bone marrow it is essential that repeated or continued treatment be given with very great care and under expert supervision. When repeated courses are given, considerable judgment is called for in selecting suitable time intervals which, in general, should not be shorter than six weeks between courses.

Side-Effects.—Reference has already been made to the local damage that may result from nitrogen mustard therapy, and to how this may be avoided. Of the general side-effects, the most common is nausea or vomiting, and the most dangerous is aplastic anæmia. Various drugs have been advocated for the prevention or alleviation of the former These drugs include barbiturates, hyoscine, antihistamines and pyridoxine. In some cases they appear to be beneficial, but in others they seem to have little effect Patients vary considerably in their reactions to nitrogen mustard, and in the writer's experience highly susceptible patients derive little benefit from any measures that have been tried, although recently some encouraging results have been obtained with promethazine chlorotheophyllinate (Avomine), the antihistamine drug introduced for sea-sickness. Chlorpromazine (Largactil) has also been recommended, in 25 mg. doses at four-hourly intervals, commencing a few hours before the nitrogen mustard.

Nitrogen mustard therapy *almost invariably causes depression in* hæmatopoiesis. All the formed elements of the blood are liable to be affected, the earliest and most constant effect being on the leucocytes. The degree and

and that the changes may range from mild hypoplasia to almost complete aplasia. It is reassuring to note, however, that these hæmatological effects tend to be transient, and that regeneration, following cessation of treatment, is usually rapid and vigorous In the writer's experience nitrogen mustard therapy has never resulted in permanent damage to the blood-forming tissues. In this respect nitrogen mustard differs from X-radiation, in which the hæmotoxic effects may be progressive and irreversible. Nevertheless, it is obviously

[illegible]

and the advent of modern antibiotics has provided an effective weapon in their prevention and management

Blood transfusions are indicated if severe anæmia develops as a result of treatment, and also as a prelude to treatment in patients who are severely anæmic before treatment There is no convincing evidence that hæmatinics are of value in preventing or correcting anæmia due to nitrogen mustard. If, however, a concomitant deficiency in iron is thought to be present, due to hæmorrhage or other causes, this should receive appropriate treatment.

ORAL NITROGEN MUSTARDS AND TEM

Certain other nitrogen mustard compounds have been prepared that are suitable for oral administration The best known of these are " R 48 ",

[illegible]

Other substances suitable for oral therapy have recently been introduced which, while differing chemically from the nitrogen mustards, are believed to exert a lethal cytological effect in the same fundamental manner. The only one available commercially is " TEM " (triethylene melamine) This drug has been used mainly in the treatment of Hodgkin's disease, lymphosarcoma and chronic lymphatic leukæmia, and has given moderately encouraging results. Its use, however, [illegible]
partic
also c
tolera
alime
parenterally When this is done, its effects are similar to those of nitrogen mustard. A further danger results from the instability of the drug so that individual samples may vary in toxicity. It is supplied by Imperial Chemical Industries in enteric-coated capsules, each containing 2 5 mg. A suggested scheme of dosage is 2 5 to 10 mg., according to body-weight, weekly, by mouth, until maximum benefit is attained, when, in the absence of signs of toxicity, a

obtained in a group of children suffering from acute and subacute leukæmia. Since then a number of observers have recorded their experiences with aminopterin and allied substances, and have confirmed that they are capable of inducing dramatic remissions in leukæmia, both in children and more rarely in

frequently, and more frequently in children than in adults In general, significant remissions may be expected in about a third of cases treated. In favourable cases the response may be highly gratifying. The blood picture returns towards normal, and may actually become normal in respect both of white cells and red cells. The sternal marrow may also show a striking reversion to normality These hæmatological effects are accompanied by an improvement in general health

nia, pyrexia, hæmorrhages and all disappear. The duration of weeks, but occasionally months. Prolonged remissions can usually be obtained only by maintenance therapy in which the dose of the drug is carefully adjusted by trial and error just short of producing toxic symptoms. Such a balance between the therapeutic and the toxic dose is difficult to achieve, and even in cases where it is attained there finally comes a time when the drug loses its effect on the leukæmic process.

The folic acid antagonists may also bring about a degree of hæmatological remission in chronic leukæmia, but the effects on the general condition have been disappointing and inferior to those obtainable with other forms of therapy.

The most promising analogues which have been found are aminopterin

preferred, since it is easier to find the dosage which will produce a good response with minimal toxic effects

should be withdrawn. If remission is obtained maintenance treatment, 5 to 10 mg. per week, is advisable. *If aminopterin is to be used the initial dose is* 0·5 to 1 mg. a day and the maintenance dose 1 to 2 mg per week

Side-Effects.—The undesirable effects of folic acid antagonists are mainly on the alimentary system and include stomatitis, ulceration of the oral mucosa,

ug must be withdrawn

blood transfusions and

ible cases, therapy may

cautiously be resumed. Liver extracts and folinic acid have been advocated to counteract the toxic effects of folic acid antagonists, but they are of no value for this purpose. Because of their unpleasant toxic reactions, and the uncertainty and brevity of their beneficial effects, many pædiatricians have abandoned the use of these drugs.

6-MERCAPTOPURINE

(Puri-Netol)

This compound is an adenine analogue which is believed to inhibit cellular proliferation by interference with purine metabolism. The biological properties of this and related substances were discovered recently as a result of systematic [illegible] cid [illegible] of [illegible] fer

Clinical trials during the past two years have shown it to be of particular value in the treatment of acute leukæmias, especially in children, partial or complete remissions of three to four months having been obtained in about a third of the cases treated Since it is less toxic it is to be preferred to the folic [illegible] It [illegible] to respond to folic acid antagonists or cortisone It is not effective in chronic lymphatic leukæmia, but recently it has been shown to produce long remissions in chronic myeloid leukæmia with a minimum of toxic effects In this condition it is doubtful whether it is as useful as Myleran, but it may be of value in cases which have become resistant to Myleran It has also proved of some value in controlling temporarily the acute terminal phases of chronic myeloid leukæmia.

Administration and Dosage.—The drug is marketed by Burroughs Wellcome in tablets of 50 mg. In acute leukæmia and in chronic myeloid leukæmia it is given by mouth in daily doses of about 2 5 mg. per kg. body-weight There may be a delay of up to four weeks before a beneficial effect is seen Subsequently maintenance treatment is necessary, the dosage being adjusted according to the hæmatological and clinical response

Side-Effects.—Overdosage may result in marrow depression and gastro-intestinal symptoms, but on the whole the drug is less liable than folic acid antagonists to produce dangerous or unpleasant side-effects

HORMONE THERAPY

CORTICOTROPHIN (ACTH), CORTISONE, PREDNISONE AND PREDNISOLONE

Soon after the advent of these substances their effect on normal and abnormal cell growth received attention, and their depressant effect upon lymphatic tissue was soon observed As a result of clinical trials it has been shown that a temporary regression may occasionally be obtained in Hodgkin's disease, lymphosarcoma and other forms of reticulosis, but the available evidence does not suggest that they are likely to be of practical value in the treatment of these diseases

Corticotrophin, cortisone, prednisone and prednisolone are, however, finding a place in the palliative treatment of leukæmias, particularly in children. It is impossible to define, with precision, their merits as compared with the

other therapeutic agents, but they have proved effective in cases where the anti-metabolites were ineffective. While all cases of acute leukæmia sooner or later become resistant to anti-leukæmic drugs, the resistance to the anti-metabolites does not implicate the hormones, and vice versa. For this reason it has been advised that the two types of therapy should not, in the first instance, be given concurrently. One should be given if the other has proved ineffectual.

and platelet counts, thus countering the risk of infection and hæmorrhage. A favourable response is usually shown by rapid clinical improvement, including the cessation of hæmorrhage, reduction in the size of the spleen and lymph glands when these are enlarged, and the reversion of the blood picture towards normality in respect of red cells, white cells and platelets. Maintenance therapy is usually necessary, but, despite this, relapse inevitably occurs after a period of weeks or months In a very few cases a remission of a year or more has been recorded. As in the case of the anti-metabolite drugs, it is impossible to predict in an individual case whether benefit will result. Children are certainly more likely to benefit than adults, and there is considerable evidence that lymphoblastic leukæmia is more responsive than the myeloblastic type. As a very rough guide, favourable responses of variable duration may be expected in up to 50 per cent. of children and in 25 per cent. of adults.

In chronic leukæmia hormone therapy is of doubtful value, and has no claims for superiority over other forms of treatment. In certain cases of lymphatic leukæmia, however, it may be of value, as for example in cases with cutaneous infiltrations, in cases with large lymphatic nodes producing dangerous pressure symptoms, in cases undergoing terminal transformations to the acute type, and in cases with secondary hæmolytic anæmia.

Administration and Dosage.—There seems to be little to choose between corticotrophin, cortisone, prednisone and prednisolone as regards their therapeutic efficacy in leukæmia, provided the patient's adrenals are healthy. In most cases corticotrophin is not preferred, since it cannot be administered orally. Prednisone and prednisolone have much less effect on sodium retention

If cortisone is used, the initial dosage for adults should be 300 mg. daily in divided doses at intervals not greater than six-hourly, and for children the dosage should be up to 200 mg daily. The dosage of prednisone and prednisolone is approximately one-quarter to one-fifth that of cortisone A clinical and hæmatological effect can be expected within four weeks and frequently occurs within two to ten days; the dose should eventually be reduced to the lowest level which will keep the patient in remission. If no response is obtained within four weeks, hormone therapy should be discontinued and the use of a cytotoxic agent considered Care must be exercised to avoid hypoadrenalism by withdrawing the hormone gradually and by giving corticotrophin gel (40 units per day intramuscularly) during the period of withdrawal and for three days thereafter. The dangers, contra-indications and other aspects of cortisone therapy are described on p. 79

SEX HORMONES

Sex hormone therapy has been tried in a variety of malignant conditions, but as a measure of established value it is at present confined to the palliative treatment of carcinoma of the prostate and of the breast

Carcinoma of the Prostate.—The earliest observation on the effect of castration on prostatic activity is attributed to John Hunter. More recently Huggins and other showed that the progress of prostatic carcinoma could be favourably influenced by castration, and that a similar effect could be achieved by œstrogenic substances The generally accepted explanation of this is that the œstrogen damps down the activity of the anterior lobe of the pituitary, and thus by restricting the supply of gonadotrophic hormone to the testes, and also perhaps of corticotrophin to the adrenal cortex, diminishes the secretion of androgens, which are necessary if the prostatic carcinoma is to flourish

Experience during the past fifteen years has firmly established the value of œstrogen therapy in inoperable prostatic carcinoma, and has shown that stilbœstrol, the synthetic analogue produced by Dodds, is the most convenient and effective preparation

With stilbœstrol a favourable result may be expected in 80 per cent or more of cases Not only is there some increase in the expectation of life but even in advanced cases there may be striking symptomatic improvement. The writer recollects one patient rendered a helpless paraplegic due to spinal metastases, who after a few weeks' treatment was literally able to get out of his bed and walk The duration of the improvement is variable, but may be expected to persist for a year or more in 50 per cent. of cases, and up to four or five years in 15 per cent.

Administration and Dosage—Stilbœstrol therapy should be commenced in doses of 5 mg. three times daily by mouth The patient should remain on this dosage for a variable period of weeks or months until a satisfactory clinical remission occurs. If necessary, the dosage may be raised to 20 mg. or more daily in order to attain a satisfactory effect. The dosage should then gradually be reduced, provided the clinical state remains satisfactory The clinical improvement is accompanied by a fall in the serum acid phosphatase level if this is raised, as it usually is in prostatic carcinoma, especially if bony metastases [illegible]

[illegible]

indefinitely

[illegible]

scrotal line, and of any scars that may be present also o

small price to pay for the benefits conferred.

Carcinoma of the Breast.—Hormones are of

of advanced and inoperable cases of mammary

emphasized that in no way should they be regarded as substitutes for surgery or radiotherapy in cases suitable for these measures.

Œstrogens.—Analogous to the influence of orchidectomy on prostatic carcinoma, ovariectomy occasionally exerts a palliative effect on breast cancer. Furthermore, it has been shown that synthetic œstrogens may cause retardation or even regression of the growth of the tumour. The results, however, have been inferior to those obtained in cancer of the prostate, favourable responses being much less frequent and of shorter duration when they do occur. Moreover, in younger women œstrogens may produce an adverse effect and accelerate the course of the disease. For this reason the œstrogen treatment of mammary cancer should be restricted to women five or more years beyond the menopause. Stilbœstrol is the drug usually employed. Its dosage is similar to that in prostatic carcinoma and is limited by the desirability of avoiding toxic effects. The serum acid phosphatase is, of course, of no help in controlling dosage. Stilbœstrol may also be of value in cases of carcinoma of the breast in males, whereas androgens are of no value.

Androgens.—Androgen therapy is somewhat more promising as a palliative measure in advanced mammary carcinoma. Although the degree and duration of the effects are uncertain and unpredictable, considerable symptomatic benefit may occur, both in younger and in older women. Cases with osteolytic metastases in the skeleton may show particularly striking subjective and objective improvement. Pain and tenderness may rapidly disappear and the osteolytic lesions become re-calcified. Other benefits include the healing of ulcerative skin lesions and relief from pressure symptoms caused by intrathoracic metastases. Unfortunately substantial improvement occurs only in about 20 per cent. of cases, and when it does occur it usually persists for only a few months, although remissions of five years or more have been recorded. Lesser degrees of improvement may be expected in a somewhat higher proportion of patients, but more than 50 per cent. are unlikely to derive any benefit. In a recent investigation by Galton it was concluded that androgen therapy offers a convenient alternative to surgical castration, but the results are probably no better.

Administration and Dosage.—The following preparations and methods of administration are available:

(1) Methyltestosterone, sublingually, 50 to 100 mg. daily for two to ten weeks. If the result is satisfactory a daily maintenance dose of 50 mg. may then be given indefinitely.

(2) Testosterone propionate by intramuscular injection, 50 to 100 mg. on alternate days for two to ten weeks. Thereafter a weekly injection of 100 mg. may be given.

(3) Testosterone in pellet form for subcutaneous implantation. Each pellet usually consists of 100 mg. of amorphous testosterone, and the recommended dose consists of six such pellets which should be implanted through a small incision in the skin of the anterior abdominal wall and should lie radially and at least 5 cm. distant from the incision. The rate of absorption is approximately 10 mg. daily, and thus necessitates a further implantation in four to six months. [illegible]

the first month of treatment, consisting of flushings and [illegible]

DISEASES OF THE ALIMENTARY SYSTEM

SYMPTOMATIC TREATMENT

Hunger; Appetite; Food Habit.—Though the words "hunger" and "appetite" are often used indiscriminately to denote a desire for food, there is good physiological evidence that these symptoms are produced by separate mechanisms. Hunger seems to denote a generally unpleasant sensation, part

cing really painful gastric contractions

Appetite is a pleasant sensation, which, if it can be said to be localized anywhere, is felt somewhere around the palate. Appetite is directed towards a particular food or taste. By "taste" we usually mean smell, since the true taste sensation is crude.

It is not clear why we eat. Hunger in the strict sense of the word, in civilized countries, plays a minor part, and it seems that we eat to a large extent by habit; and this habit continues even if we cannot "taste" food, as after the destruction of all sensation of smell by a fracture of the skull. Emotional disturbances may also upset our normal food habits.

In disease, loss of desire for food, described by the patient as loss of appetite, may occur in acute inflammation of the stomach which affects motility; this is exemplified in the complete anorexia seen in certain types of influenza. This anorexia spontaneously disappears as the inflammation subsides. If the stomach is infiltrated with carcinoma, all movements may cease and the loss of hunger sensation may be absolute.

Psychological conditions such as grief, depression or anxiety may be accompanied by a lack of desire for food. It may be noted, on the other hand, that occasionally patients find a relief from tension in eating food and therefore eat more when they are anxious and wor

order

act by

what it feeds on. Insulin has been given, 10 units three times a day, twenty minutes before meals, with the intention of producing a mild hypoglycæmia and increased gastric motility. It is not usually very effective, but is worth trying. Methyltestosterone, 10 mg. daily, given sublingually, may help the patient to regain weight. A senile depression, which may develop in an elderly patient after an operation and diminish his food intake, may sometimes be successfully treated with amphetamine, 5 to 10 mg twice daily. This is somewhat paradoxical, as in the normal person amphetamine reduces the desire for food.

The child who refuses to eat can usually be successfully treated by making him have his meals with other children. That we all eat better in company seems an almost universal biological phenomenon. It is impossible, for example, to fatten a solitary hen.

itself requires no treatment This feeling of fullness is also a symptom of carcinoma of the stomach when the organ is incapable of dilating. It may also be noted after a partial gastrectomy It should be explained to such a patient that his gastric capacity is considerably reduced and that he must re-educate his stomach to take adequate quantities of food This may require considerable perseverance, and the effort is particularly important if he is engaged on heavy manual labour and needs a large intake of food to maintain his weight and strength.

Nausea.—Nausea is usually a symptom either of disease in the upper part of the gastrointestinal tract or of disease of the central nervous system or the inner ear. Disease of the colon or rectum does not readily give rise to nausea or vomiting, which are more likely to be produced by some obstruction in the small intestine or an inflammatory focus in the abdomen, e g. a peritonitis Irritation of the biliary tract and the pancreas readily gives rise to nausea

The treatment of nausea depends on its cause, but simple methods may suffice in mild cases. Nausea, for instance, may occur paradoxically as an accompaniment of hunger and will disappear if the subject forces himself to eat Similarly, motion sickness may sometimes be prevented by the subject forcing himself to eat in spite of nausea. For the treatment of nausea, whatever the cause, one of the most valuable drugs is chlorpromazine, 25 to 50 mg. as required.

Heartburn.—Heartburn may be defined as a burning sensation felt behind the sternum which may be accompanied by regurgitation of stomach contents

acid is the most frequent irritant it is not the only stimulus, as heartburn may occur following a total gastrectomy when the œsophagus is anastomosed to the small intestine, and any fluid regurgitated is alkaline. The treatment of heartburn is the treatment of its cause, e g. peptic œsophagitis with hiatus hernia (p. 477) Even when no œsophageal lesion can be detected, the symptom usually responds to antacids, e g compound powder of magnesium trisilicate, 4 g

Flatulence.—It is not clear what "flatulent dyspepsia" really means.

sanction; in the wet state in the gut charcoal is quite inactive. The treatment of the distended coils of gut in intestinal obstruction is dealt with elsewhere.

DISEASES OF THE MOUTH

Routine clinical examination of the mouth has been carried out since the earliest days of medicine, and such examination may yield evidence of general diseases or disorders, or signs of inflammations of the mouth of purely local origin.

The Tongue.—It used to be taught that a coated tongue was an indication of disease of the gastro-intestinal tract, but there is little satisfactory evidence to support this hypothesis. The coated tongue is due to unduly long papillæ in which food and bacterial and fungal debris become entangled. If the tongue needs treatment, it is best cleansed mechanically with a toothbrush after the teeth are cleaned.

Sometimes the filiform papillæ become exceptionally long and black; the condition is then known as black hairy tongue, and the patient may require reassurance that the condition is not pre-cancerous. It can be treated by swabbing with a 10 per cent. solution of salicylic acid in 90 per cent. ethyl alcohol, and then rinsing the mouth with a 10 per cent. solution of sodium bicarbonate. This removes some of the papillæ. An acute painful red tongue (acute glossitis) is seen in about 5 per cent. of cases of pernicious anæmia in relapse. Chronic atrophic glossitis, pale smooth tongue, is frequently seen in both pernicious anæmia, when it will respond to cyanocobalamin, and iron deficiency anæmia, when it will respond to iron.

Leucoplakia, which is usually regarded as a pre-cancerous condition, is a type of chronic inflammation of the tongue and oral mucosa. In its fully developed state it presents as whitish well-defined patches of thick consistency.

should be treated if present and any causes of local irritation should be removed. The lesion should then remain under regular observation and biopsies should be taken of any area suspected of undergoing malignant change. If carcinoma supervenes, treatment is either by irradiation or surgical excision.

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Ascorbic acid deficiency affects principally the gums, which become hypertrophied and spongy and bleed freely. The condition responds rapidly to treatment with ascorbic acid. Blood diseases, such as agranulocytosis, leukæmia and purpura, may present with signs in the mouth. In measles, scarlet fever, chickenpox and smallpox the eruption may be found in the mouth. In angioneurotic œdema the tongue and glottis may become swollen, and occasional fatalities have occurred in consequence. The condition should be treated with injections of adrenaline, 0·5 ml, and an injection of mepyramine maleate, 100 mg. Many drugs which cause skin rashes may also affect the mouth, producing redness, swelling and vesiculation. These lesions result from hypersensitivity or idiosyncrasy or from overdose. Examples of such drugs are cincophen,

barbiturates, bromides, iodides, phenacetin, phenolphthalein, salicylates and sulphonamides. Phenytoin, given for epilepsy, produces a curious overgrowth of the gum margin.

Changes in the mouth can be produced by heavy metals such as mercury, bismuth, lead, silver, gold and arsenic, but none of these, with the possible exception of gold, are widely prescribed today. Treatment of such poisoning consists in stopping the offending drug Dimercaprol (BAL) is effective in mercury, arsenic and gold poisoning; it may be of some value in bismuth poisoning; it is ineffective in the treatment of argyria, while in lead poisoning it is said to do harm It is given by intramuscular injection (see p. 282).

Certain skin diseases may manifest themselves by oral lesions, as in lichen planus, lupus erythematosus, pemphigus and herpes simplex. Herpes zoster is uncommon inside the mouth.

Syphilis can affect the mouth as a primary, secondary or tertiary lesion, though in this country this disease is now becoming extremely uncommon. Tuberculosis may also affect the tongue, but this manifestation is now very rare. A mild stomatitis is not infrequently seen due to a combination of oral sepsis, tobacco smoking and alcoholism It responds to removal of the irritant causes.

Aphthous Stomatitis.—This condition, which is extremely common, is characterized by outbreaks of small erosions of the mucosa surrounded by erythema. These ulcerations sometimes appear in response to some particular food, sometimes in association with menstruation, sometimes in response to stress and often for no apparent reason. The lesions are extremely painful. Innumerable forms of treatment have been recommended both to heal the lesions and to prevent recurrence Ten per cent silver nitrate may be applied locally to the ulcers, and pain may be relieved by sucking a tablet containing amethocaine. In some cases cortisone, 50 to 100 mg. daily, appears to abort an attack.

the association of two organisms, a fusiform bacillus and a spirochæte. It usually originates in a septic mouth and produces small grey ulcers which enlarge and coalesce.
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organisms are sensitive to penicillin, and the condition responds to injections of this drug. *Penicillin may also be given locally in the form of lozenges.*

The Teeth.—In the past the theory of infective foci was used to explain the ætiology of many diseases and the teeth were often incriminated. This era has fortunately passed and wholesale extractions are no longer carried out

to ill-fitting dentures.

atropine, as in the treatment of peptic ulcer (see p. 481). These measures will relieve the symptoms of a mild case.

The symptoms may, however, be more severe as the *peptic œsophagitis* becomes more chronic and less amenable to medical treatment, and may be associated with actual ulceration and bleeding. Such œsophageal ulcers are small and shallow and are not easily detected radiologically, but are seen endoscopically. If they bleed, the treatment is the same as that for hæmorrhage from the stomach or duodenum, though the bleeding is not usually severe.

The more radical surgical treatment is to reconstitute the sphincteric action at the cardia and thus prevent regurgitation, or, as in duodenal ulcer, to resect a major part of the stomach in order to reduce permanently its output of acid juice. Both these methods of treatment have their advocates. The reconstitution of the sphincteric mechanism by reduction of the hernia appears simple, but the operation has not infrequently been followed by recurrence. The more radical and perhaps more rational method of treatment is to attack the source

claimed for the operation of partial gastrectomy accompanied where necessary by dilatation of the stricture by bougie.

Cardiospasm (achalasia).—This condition is now less common than formerly; the difficulty in swallowing is due to spasm at the cardiac sphincter. The ætiology is unknown, but a very similar condition may appear after vagotomy, though it is then usually transient. Cardiospasm presents a typical picture on radiological examination and endoscopy may show some œsophagitis due to retention of food. It may persist intermittently for years and can cause great distress and disruption of social life as the sufferer may not dare to eat meals outside his own home. Enormous distention of the œsophagus may ultimately occur, so that the organ may be mistaken for a mediastinal tumour. Though it is possible to relax the sphincter temporarily with nitrites, the results achieved are seldom satisfactory. In the early stages, however, if the spasm is episodic it is worth trying glyceryl trinitrate tablets, 0·5 mg. ($\frac{1}{120}$ gr.), sucked under the tongue. One tablet should be taken at the beginning of a meal and another half an hour later.

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(Negus') under either loca.

found that the mercury bougies originally recommended by Hurst are less effective. Hydrostatic dilatation can be repeated, but if after two sessions relief is not achieved, surgical intervention should be advised. A satisfactory operation should aim at relieving the spasm while maintaining the action of the cardiac sphincter, and thus preventing regurgitation of stomach contents into the œsophagus. An operation originally designed by Heller which divides the circular fibres of the cardiac sphincter seems to fulfil these desiderata. Anastomotic operations which bypass the sphincter are contra-indicated, since they may be followed by severe œsophagitis.

There is no doubt that emotion can cause sufficient spasm to produce dysphagia in some people, but it is doubtful if this ever gives rise to narrowing due to structural changes. It can however augment the effect of pre-existing organic disease and the sufferer is then apt to ascribe the dysphagia entirely to

emotional causes Thus dysphagia from peptic œsophagitis may appear to be

have spread from the stomach.

Radical treatment consists of resection of the growth and anastomosis of the remainder of the œsophagus to the stomach or the intestine. Advances in thoracic surgery have enabled surgeons to undertake such operations with reasonable hope of success. A sufficient number of three- or five-year " cures " have been reported to justify advising the operation in selected cases. Following an operation in which the reservoir function of the stomach is lost, the patient may experience the same difficulties in maintaining nutrition as occur after the operation of gastrectomy and will require the same type of treatment and

prior to operation, it should not be used as a palliative as it only prolongs the discomfort of a miserable life

Corrosive Œsophagitis.—This can occur following the swallowing of a substance such as Lysol Many years ago Lysol was frequently taken with suicidal intent, but there are now other more attractive poisons. It may, however, be taken accidentally and causes intense inflammation in the œsophagus with subsequent stricture formation In the acute stage the patient requires morphine for the pain, and no attempt should be made to pass a stomach tube as the danger of perforation of the œsophagus is very great Water and electrolyte balance must be maintained until the inflammation subsides In some cases a temporary gastrostomy may have to be made Subsequently dilatation of the resulting stricture, or more rarely its resection, may be necessary.

DISEASES OF THE STOMACH

PEPTIC ULCER

Peptic ulcer occurs in those sites to which pepsin and acid have access, and it is reasonable to suppose that the ulcer is due to peptic digestive action. Since, however, normal stomachs do not undergo digestion, we must postulate some opposing mucosal resistance Rational treatment should therefore be directed towards decreasing the secretion of acid and pepsin, or increasing in some way the resistive power of the mucosa.

Usually duodenal ulcer is associated with higher outputs of acid and pepsin than normal, and these high secretions continue during the interdigestive periods

received much more attention than the unknown factors responsible for mucosal resistance.

The treatment of peptic ulcer has to be considered *under three headings*: the treatment of symptoms; the healing of the ulcer; and the prevention of a recurrence of the ulcer. Relief of symptoms does not necessarily mean that the healing of the ulcer has occurred. Complete loss of symptoms may be accompanied by persistence of the ulcer niche for many weeks or even months; the ulcer may ultimately heal or be associated with a recurrence of ulcer symptoms. Similarly, the disappearance of the ulcer niche in no way guarantees that the

urn. In general, it may be said

it is probable that the healing of an ulcer can be hastened, but it seems very doubtful if there are therapeutic measures which will alter the natural course of the ulcer disease, with its tendency to relapse and remit.

Uncomplicated Gastric and Duodenal Ulcer

Rest in Bed.—There are good clinical grounds for advising rest in the treatment of ulcer, although it is not clear wherein the benefit of rest lies. Mild degrees of ulcer pain will respond rapidly to this measure alone. When pain is more severe, rest in bed may be essential if relief is to be obtained. It need not be complete and the patient can take baths and use the toilet. If relaxation is not possible at home, the patient should be treated in a hospital or nursing home. Rest in bed should be insisted on if there is considerable pain with much tenderness and rigidity, as perforation or hæmorrhage may in such cases be prevented.

Diet.—It is often said that meals should be frequent, should be mechanically non-irritating, chemically non-stimulating, and easily digested, but it is not easy to find experimental evidence that this advice expedites healing. Much dietetic therapy in the therapeutics of peptic ulcer is traditional and rests on no rational basis; there are only a few principles to guide us. The diet should clearly be adequate in calories and vitamins On the original Sippy régime, for *instance, the patient regularly lost weight.* Not infrequently a patient with a gastric ulcer will present with evidence of weight loss and malnutrition, and the nutrition of such patients will benefit from adequate feeding. In addition, there is some evidence that a gain in weight is associated with a more rapid tendency to heal.

Of the [illegible] in the diet, since f [illegible] be given, or ascorbic acid 100 mg [illegible] certainly a powerful stimulant to gastric secretion, and there is therefore some [illegible] certainly

with most patients.

The effect of smoking on peptic ulceration is not clear. Though clinical [illegible]

he then acts accordingly. If no beneficial effect is produced, smoking can be resumed if the patient so desires.

Drug Treatment.—*Antacids.*—Antacids have been given for more than a century Symptomatically they relieve ulcer pain Their use also rests on the assumption that since acid and pepsin are essential for ulcer formation the neutralization of acid will necessarily aid healing. This does not necessarily follow, since this argument assumes that the healing process is the reverse of the ulcerating process Furthermore, it is known that healing may proceed satisfactorily in the presence of acidity in the stomach.

The antacids which have been used include sodium bicarbonate, magnesium oxide, hydroxide and carbonate, calcium carbonate, bismuth carbonate, aluminium hydroxide and magnesium trisilicate. Sodium bicarbonate is an absorbable alkali, and if given in large amounts, particularly if defective renal function is present, it can readily produce alkalosis For this reason it is now less frequently prescribed alone Magnesium oxide, hydroxide and carbonate are all effective antacids, but tend to act as aperients, an action which may be undesirable. Calcium carbonate has the opposite effect of constipating the patient Bismuth salts have been used in the past, but are very feeble antacids and there seems no rationale for their use unless they have some pharmacological action which is as yet unrecognized The danger of alkalosis from the widespread use of absorbable alkalis such as sodium bicarbonate resulted in a search being made for effective antacids without this disadvantage Aluminium hydroxide and magnesium trisilicate act as antacids, but the exact chemical mode of action is not a pure neutralization but is more complex.

Aluminium hydroxide given orally as Aluminium Hydroxide Gel (B P.C.), 4 to [illegible]

prescribing liquid paraffin or by giving magnesium salts in the mixture. Magnesium trisilicate, 1 to 4 g., has somewhat similar antacid properties to aluminium hydroxide

Antacids differ not only in the total amount of acid they can neutralize but also in the rate at which they carry this out Different criteria of estimating effectiveness are therefore possible There are also important differences due to the physical form in which the antacid is presented, tablets, which do not break up readily, are much slower in their action than solutions. No matter which antacid is prescribed, there seems no doubt that by giving it in repeated doses it is possible to maintain a pH in the stomach greater than 4 0, that is, a level at which pepsin tic activity ceases. There is, however, little evidence that healing of an ulcer is thereby hastened It would seem that a mixture of antacids should be prescribed For this purpose Pulv. Mag Trisil Co. (B.P C) is frequently suitable, since it contains equal parts of magnesium trisilicate, heavy magnesium carbonate, chalk and sodium bicarbonate—that is, rapidly acting as well as longer acting antacids In an acute case of active ulceration, half a level teaspoonful (2 g) can be given hourly in water or milk; in milder [illegible]

gastric milk drip may be tried.

Continuous neutralization can be achieved by an intragastric drip of milk to which has been added an antacid, such as sodium bicarbonate, 1 g. to 300 ml. milk. The drip is continued night and day for several days. During the twenty-four hours 3,600 ml. of milk are given, that is, at a rate of 2·5 ml. a minute, a total of 2,400 Cals. in all. Aluminium hydroxide has also been added to the milk in place of the sodium bicarbonate, though paraffin will then be necessary to treat the resulting constipation. This therapy is less trying to the patient if a very small soft latex or plastic tube is used for the intranasal feeding.

Technique.—The doctor who passes the tube will better appreciate the details of technique if he is accustomed to passing it on himself. Intranasal introduction is far preferable to peroral. One side of the nose has usually a freer airway than the other, and this side should be chosen. If necessary the passage can be inspected with a nasal speculum. The nose is then anæsthetized with 1 ml. of 2 per cent. amethocaine dropped into the nostril, and if the head is thrown back the pharynx also becomes anæsthetized. The patient should then sit upright with the head erect, and the tube, lubricated with liquid paraffin, is [illegible] horizontally backward along the floor of the nose. It is [illegible]

œsophageal sphincter. At this stage the patient should gently take a sip of water, and as the swallowing movement occurs, the sphincter relaxes and the tube slips into the œsophagus. If the patient now sips water, peristalsis will carry the tube into the stomach. Where practicable, it is advisable to "screen" the tube in position in the stomach to avoid the danger of œsophageal feeding.

Sedatives.—Whatever the ætiology of peptic ulcer may be, there seems no doubt that the sedation of the higher centres has a beneficial effect and it is unnecessary to speculate through what pathway this acts. Phenobarbitone is widely used for this purpose, and some experienced practitioners believe it to be the most valuable drug in the treatment of ulcer. It is particularly useful in [illegible] patients with duodenal ulcer in doses of 15 to 30 mg. (1/4 to 1/2 gr.) [illegible] the patient should always be [illegible] treated with suitable hypnotics. [illegible] is therefore contra-indicated. [illegible] rates [illegible] tone, 0·25 to 0·5 g. (4 to 8 gr.). If the patient [illegible] during the night, a longer-acting hypnotic is indicated, such as amylobarbitone or butobarbitone, 0·1 to 0·2 g. (1½ to 3 gr.) The development of a tension state sometimes precedes the breakdown of an ulcer, and if the patient can recognize this, prophylactic sedation may be of gre[illegible]

Parasympathetic Depressants. [illegible] given in sufficient doses can be shown to exert a pharmacological a[illegible] the stomach. To achieve definite effects it is [illegible] to increase th[illegible] toxic effects appear and then to reduce it. [illegible] of belladon[illegible] ient [illegible] since the dose may be read[illegible] Patients [illegible] their [illegible] atropine, and some who n[illegible] s before toxic [illegible] ost useful in [illegible] the sufferer [illegible] dose should [illegible] about 3 ml.

(45 min) and can be raised steadily until there is dryness of the mouth and blurring of vision on waking, when it should be slightly reduced. By day such large doses are quite impracticable for the ambulant patient as they interfere

undesirable side-effects. Some of these drugs are derivatives of the alkaloids of belladonna. Most are synthetic substances with no relation to the chemical structure of atropine, but their general effect is to simulate a para-sympathetic depressant action, that is, they tend to inhibit motility of the stomach and intestine and depress secretion Examples of such drugs are hyoscine butylbromide (Buscopan), methantheline (Banthine), propantheline (Probanthine), oxyphenonium (Antrenyl), penthienate bromide (Monodral), diphenmethanil (Prantal), tricyclamol (Lergine) All of these substances can

will be necessary to determine the ultimate place of these drugs in the treatment of gastro-intestinal disease in general and peptic ulcer in particular. Until this has been obtained it is not possible to recommend unequivocally any of these preparations as superior to preparations of atropine or belladonna

Surgery.—There is no doubt that surgery has an important place in the treatment of peptic ulcer and its complications. Emergencies such as perforation or bleeding clearly may come within the surgeon's province, as does chronic pyloric obstruction. In addition, patients in whom ulcer dyspepsia has repeatedly returned and for whom the resources of medical treatment have afforded no lasting relief are candidates for surgical treatment. The decision to advise surgery largely rests on an assessment of the intractability of the dyspepsia and the disability it causes The length of time a patient has taken off work is no certain indication, since some conscientious patients, who ultimately greatly benefit from surgery, remain at work despite much discomfort. Objective signs that aid the physician and surgeon in coming to a decision are the radiological appearances which should show either an undoubted ulcer in the stomach or duodenum or a grossly deformed duodenal cap Tests of gastric secretion are helpful in a case with duodenal ulcer If the stomach produces very large amounts of acid to a maximal histamine test, experience shows that permanent

The objections to surgical treatment are that even in the most skilled hands there is a mortality which can never be entirely negligible and that operation does not provide an absolute guarantee of freedom from symptoms. A proportion of patients after operation for ulcer develop a post-gastrectomy syndrome which can give rise to as much disability as the original ulcer. Operation, therefore, should never be advised lightly. Very important to the outcome of the operation is the attitude of the patient, a robust, determined outlook spells success. While the choice of operation is naturally the prerogative of the operating surgeon, the physician should be aware of the various possibilities that surgery affords For an intractable duodenal ulcer, subtotal gastrectomy is a

highly successful operation; the alternative is vagotomy combined with gastro-enterostomy. The latter operation is less radical and may be indicated in women with chronic duodenal ulcer in whom the

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ulceration in a proportion of patients, so that nowadays it is usually combined with vagotomy. The advantage of such an operation is that the stomach reservoir is left intact. It may also be argued that a gastrectomy could always be performed at a later date should the simpler operation of vagotomy and gastro-enterostomy fail.

Complications

Hæmatemesis and Melæna.—A large number of peptic ulcers bleed at some time in their history, as demonstrated by the presence of occult blood in the stool. Such bleeding constitutes no serious danger. Severe bleeding, however, fro

rest

from varicose veins secondary to portal hypertension. The commonest causes of gastro-duodenal bleeding are acute and chronic peptic ulcers; massive bleeding from a carcinoma of the stomach is relatively rare. Bleeding from the

that red blood appearing from the rectum can come from a duodenal ulcer, since if bleeding is sufficiently profuse it can pass through the intestine in a matter of minutes before any chemical change has time to occur.

The immediate treatment of a patient who has had a severe hæmorrhage is the injection of morphine, 15 mg. (¼ gr.), to allay anxiety. The patient should be put to bed and a record maintained of temperature, of the hourly or half-hourly pulse rate and of four-hourly blood pressure readings. The practitioner will have to decide whether to transfer the patient to hospital. Factors which influence prognosis, and therefore his decision, are as follows. The age of the patient is the single most important factor in prognosis. Under thirty-five, very few patients will succumb even without transfusion; the older the patient, the greater the risk from bleeding. Bleeding which presents as melæna is not so dangerous as bleeding which presents as a hæmatemesis. The extent of the bleeding is

A decision may have to be made about transfusion. Apart from a visual estimate of the blood lost in the vomit or stool, there is no simple method of estimating the extent of the bleeding, unless considerable laboratory facilities are available. The fallacies of hæmoglobin estimations for the assessment of continuing bleeding are obvious, and it is therefore necessary to rely largely on clinical

The single most useful index is the pulse rate. If

wrist or seen in the neck, and the blood pressure cannot be detected, blood transfusion is still indicated, since it is possible to revive such a patient by massive transfusion and later to save life by gastrectomy.

When the patient has spontaneously recovered from his hæmorrhage, or has done so with the aid of a blood transfusion, the question of feeding him arises.

lives, a minority of cases can be saved only by surgical treatment. Surgery is undoubtedly the most direct method of dealing with hæmorrhage. It is indicated particularly in older patients, since it is in such patients that hæmorrhage is apt to continue, due to the rigid non-contractile vessels. The particular site for gastric ulcers which tend to bleed severely is high up on the posterior wall of the stomach, where the ulcer is in proximity to branches of the left gastric artery It should be realized that it may be impossible at laparotomy to detect an ulcer by palpation, and it is even possible for the patient to bleed to death from an ulcer that the surgeon cannot find In such cases a " blind " gastrectomy has to be done

Perforation.—An important emergency of peptic ulcer is that of perforation. This may occur with a peptic ulcer of the stomach or more commonly of the duodenum , it may also rarely occur with a carcinoma of the stomach The onset of the condition is usually dramatic and the diagnosis is seldom in doubt Sometimes the condition is suspected, but further signs of peritonitis fail to develop. This may be due to the perforation being rapidly sealed off, thereby preventing any further leak of gastric contents

required in a high proportion of cases Other surgeons favour conservative treatment, since they consider that, provided fresh material is prevented from

connected to some type of pump which will maintain continuous suction

Procaine benzyl penicillin (B.P.), 300,000 units daily, and streptomycin, 0·5 g. twice daily, are given parenterally. Water and electrolyte balance must be maintained by intravenous infusions of electrolyte and glucose solution (p. 103). It is usually possible to discontinue these infusions after about three days, when the perforation may be presumed to have become sealed. A fluid [illegible] be given by mouth for [illegible] week, after which the p[illegible] experienced hands it se[illegible] the mortality from this method is no greater than by the ordinary orthodox method of suture. It requires, however, more prolonged care and gives rise to more anxiety. It is, of course, always possible that a carcinoma might be missed if this conservative treatment is employed.

Cogent evidence has recently been put forward that a distinction should be made between the perforation of an "acute" peptic ulcer, that is, one in which there has been no previous history of dyspepsia, and the perforation of a "chronic" peptic ulcer where there has been a definite history of prolonged dyspepsia. The "acute" perforation should be treated conservatively without operation, as already described, since it will close spontaneously, while the "chronic" perforation should be treated as for a chronic ulcer, that is, by partial gastrectomy. There is much to recommend this view, but these results require confirmation before this management can be recommended as the treatment of choice. In any case, it is now quite clear that the great majority of perforations can safely be treated conservatively. This might indeed be the preferable treatment [illegible]

P[illegible]

is stenosis The condition is usually called pyloric stenosis, though most frequently the site of [illegible]

made by a skilled radiologist, though gastroscopy may be of some help. In order to get an accurate radiological picture it is necessary to wash out the stomach and aspirate all fluid contents before the patient undergoes radiological examination.

The task of washing out a stomach is commonly delegated to a junior nurse, though it is really a skilled procedure Only those who have washed out a badly obstructed stomach and then observed the result by gastroscopy know how difficult it is to render a stomach clean. Since the patient has to swallow a large [illegible] on the pharynx, i.e with the patient lying on his back. The warmed and lubricated tube is then passed. The stomach should be sucked as dry as possible, using the old-fashioned Senoran's evacuator, which is a simple and effective instrument. Warm saline should be gently run into the stomach from a funnel, which should not be raised higher than necessary. When ½ to 1 litre of fluid has run in, the funnel is lowered and the fluid runs out into a bucket; the last few ounces should be aspirated with the evacuator. The process is repeated until the washings become clear Frequently, if there is much residue in the stomach, the tube becomes blocked and may have to be withdrawn, cleared and passed again. The fluid that is introduced into the stomach only washes over the surface of the residue in the stomach and slowly loosens it. The process of

extracting the residue is therefore tedious to the physician and tiring to the patient.

If the stenosis is considerable and there has been much vomiting, the fluid intake and output of the patient should be recorded on a chart. The diet given should initially be entirely fluid and the stomach should be aspirated daily.

If there has been vomiting of any severity, dehydration occurs with the loss of sodium, potassium and chloride. The principles of replacing fluid and electrolyte loss is discussed elsewhere (p. 96). The administration of parenteral fluid is always necessary in moderately severe or severe pyloric obstruction. Normal saline solution provides the necessary sodium and chloride, potassium salts being given in addition, either by mouth or by adding them to the infusion. Electrolyte concentrations in the blood should be periodically measured and recorded. It is possible to restore the electrolyte balance of even the most severe case before operation. In pyloric stenosis, particularly, there may occur a great drain of potassium from the cells, which may be reflected in a low serum potassium. Potassium deficits of up to 1,000 m.Eq. can develop, that is, equivalent to 75 g. potassium chloride. Potassium therapy has to be very prolonged to replace losses of this magnitude, but fortunately a clinical response occurs long before complete replacement is achieved. Various potassium salts are available for treatment, but potassium chloride is the one recommended. It should be given by mouth in doses of 4 to 8 g. a day, i.e. 50 to 100 m.Eq., according to the potassium deficit estimated.

Antispasmodics are often given in cases of pyloric stenosis, and though they tend to relax the pylorus, they also inhibit gastric movements. The stomach therefore does not necessarily empty more freely and dramatic results cannot be expected when the obstruction is mainly due to structural change. Atropine in the form of tincture of belladonna is probably absorbed from the stomach and can be given in increasing doses, as already described.

Once the stomach has been emptied and the fluid and electrolyte loss of the body replaced it is possible to judge from the clinical state the gain in weight and the fluid balance chart whether the patient is retaining fluids, so that parenteral therapy can be discontinued and the diet slowly increased. There is frequently an early and rapid gain in weight, indicating rehydration. If the gastric residue diminishes, it is clearly a sign that the stenosis is lessening and the diet may be increased with the addition of puréed foods. Eventually almost normal gastric emptying may return and the patient may be able to maintain health and strength provided continual care is taken with his diet. If the patient is prepared to live in this way, there is no immediate need for any operation. The course of the stenosis may, however, proceed differently. Following the initial gain due to rehydration, weight continues to be lost. In addition, the failure of the volume of the gastric aspirates to diminish shows that the stenosis is not yielding to treatment. In such a case operation becomes imperative and only its timing is a matter for discussion. Once a patient is rehydrated and electrolyte losses have been replaced, operation should not be further delayed. Prior to operation it is desirable to give the water-soluble vitamins, including ascorbic acid. The operations to be considered for stenosis due to peptic ulcer are gastro-enterostomy, with or without vagotomy, and partial gastrectomy. The choice between these may be influenced by the response of the stomach to a maximal histamine test.

Post-Gastrectomy Syndrome

After gastrectomy and less frequently after gastro-enterostomy, a train of symptoms may appear which is sufficiently definite to be recognized as a syndrome. These symptoms consist of weakness and palpitation, flushing, sweating and drowsiness. The syndrome is classified as early or late according to its occurrence either soon after food or after the delay of an hour or hour and a half. The most probable explanation of the early symptoms is that they are due to stimulation of the small intestine by stomach contents, the stimulus being mechanical, thermal or due to hypertonicity of the fluid. The late symptoms are identical with those of hypoglycæmia. It is important to emphasize that any of the symptoms mentioned above can occur in a normal person, but they seem to be more common in patients with duodenal ulcer even though no gastrectomy has been performed. They are therefore to be considered as an exaggeration of a response to food which occurs in many normal people. If diligently searched for, these symptoms will be found in a great number of patients after gastrectomy, but they are only severe in a very few. There seems no doubt that the symptoms are more severe or are complained of more readily in the reactive type of patient.

Prevention.—If some of these symptoms follow operation, the patient may be disappointed if he has been led to expect a complete cure and has not been warned of this possibility. Accordingly it is wiser, when discussing a proposed ... but instead to talk of the

... it. By this means

... these symptoms

after operation.

... are often helped by any

...

of milk before each meal. Lying down after a meal delays gastric emptying in many patients and may prevent symptoms. Unduly hot fluids can produce

...

increased to 25 mg. until a satisfactory effect is obtained. If the drug is effective by injection, it may be given orally, when a dose of 125 to 500 mg. will be necessary as it is so poorly absorbed. The side-effects of hexamethonium therapy are discussed elsewhere (p. 589).

The late syndrome, which is identical with that of hypoglycæmia, only comes on if the subject exercises after a meal; it may be sufficiently severe to provoke loss of consciousness. It is relieved by sugar.

Loss of weight and muscu... is a common complaint. In a patient engaged ... e the ... mon

... intake of food, and this defect is

... who requires to eat large amounts

of food to maintain his weight and strength. Gain in weight can only be achieved by eating more concentrated foods such as fats, eating at more frequent intervals, and above all by resolutely forcing the stomach to take the quantities of food that are required. The practitioner must continually encourage the

patient to do this. A patient who requires large amounts of food should be warned beforehand of the possible effects of the operation.

GASTRITIS

The concept of gastritis has undergone many vicissitudes during the last century. Owing to the careful histological examination of stomachs by Faber and others, whose findings have been confirmed by methods of gastric biopsy, it is generally agreed that gastritis is extremely common. Inflammatory changes confined to the gastric mucosal layer apparently cause few symptoms which may be in marked contrast to the gross changes in appearance of the stomach. All attempts to find a definite symptom complex corresponding to the histological appearances of acute or chronic gastritis have failed. Hence gastritis must be considered to be more of a histological than a clinical concept.

It is recognized, however, that acute inflammation of the stomach may arise in the course of a fever, the most profound change being observed in influenza. Chemically irritant drugs or the toxins of the staphylococcus all give rise to gastric inflammation. Corrosive gastritis from a chemical irritant is the most extreme example. Gastritis in the course of an infection will abate with the fever, though it is said that the histological changes persist for some time after defervescence. The accompanying anorexia or nausea will prevent the patient from taking anything more than a fluid or very light diet. As appetite returns, the diet will naturally be increased. Gastritis due to a staphylococcal toxin is a severe self-limited disease of short duration. If vomiting and diarrhœa are prolonged, fluid and electrolyte replacement may be necessary (p. 103). If an irritant poison has been swallowed, the stomach should be washed out and the appropriate antidote introduced (see p. 850).

Chronic gastritis can be recognized by histological examination, but as with acute gastritis no typical clinical picture can be delineated. The diagnosis is sometimes made in a patient who complains of vague dyspeptic symptoms and in whom no ulcer or other lesion can be detected radiologically. Such a diagnosis rests on no secure ground. Possible measures that may help such a patient are to ensure that he has no septic teeth and that he moderates any excessive smoking or drinking.

An atrophic gastritis exists which can be seen histologically in contiguity with a gastric ulcer or a gastric carcinoma, but no treatment is required apart from the treatment of the ulcer or the cancer itself. It has been suggested that atrophic gastritis is a pre-cancerous lesion, but this hypothesis has not been adequately established. There is, finally, an absolute atrophy in the stomach which occurs in Addisonian pernicious anæmia, or may follow prolonged inflammation. In either case a megaloblastic anæmia may ensue. The atrophic state itself gives rise to no symptoms and requires no treatment. There is some evidence that the atrophic gastric change found in pernicious anæmia is a pre-cancerous state, and since such patients are under frequent hæmatological observation it would be wise to arrange for radiological examination should they complain of unexplained dyspeptic symptoms subsequent to the restoration of their blood picture to normal.

CARCINOMA OF THE STOMACH

Radical treatment of carcinoma of the stomach is the province of the surgeon, once the decision to operate has been made, everything should be done to

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Prevention.—If some of these symptoms follow operation, the patient may be disappointed if he has been led to expect a complete cure and has not been warned of this possibility. Accordingly it is wiser, when discussing a proposed operation with the patient, not to use the word " cure " but instead to talk of the degree of relief to be expected, e.g. 80 per cent. or 90 per cent. By this means patients are less disappointed should they experience some of these symptoms after operation

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improve the condition of the patient. If there is pyloric obstruction and there has been much vomiting, water and electrolyte replacement will be required; the anæmia which is frequently present may require transfusion. It does not

palliative partial gastrectomy if there has been previous obstruction, even if secondary growths are disclosed. If resection is not possible a gastro-enterostomy may bring some relief. Total gastrectomy is now technically possible. It necessitates the anastomosis of the œsophagus to the jejunum with loss of the reservoir function of the stomach. This loss leads to obvious difficulties in maintaining nutrition, and the value of such extensive operations which naturally carry a relatively high mortality is not yet decided. There is also a total loss of Castle's intrinsic factor, so that pernicious anæmia will develop if the patient survives for more than two to three years. Hence injections of cyanocobalamin should be given. Radiotherapy for carcinoma of the stomach seems ineffective. If no surgical treatment is possible, the management of the patient follows that of all inoperable cancers, and opiates and sedatives to relieve pain and anxiety should not be spared

DISEASES OF THE INTESTINES

INTESTINAL OBSTRUCTION

While this condition is rightly the province of the surgeon, it can present as an acute abdominal emergency either in family or in hospital medical practice.

since

may

bowel.

The commonest causes of (1) are hernias, adhesions from a previous operation,

of (2) is a peritonitis

a perforated peptic

abdomen, but this is of no clinical import

The distinction between the paralytic and the mechanical types of obstruction can normally be made on the history and the presence or absence of colicky pain, while the presence or absence of bowel sounds on auscultation is particularly helpful.

In all doubtful cases a surgical colleague should be consulted. Exploratory operation is imperative in mechanical and closed-loop obstruction, or where there

it may be considered wiser to observe the

ment is the rule. The general principles of treatment are to decompress the gut, to replace water and electrolytes lost, to maintain nutrition and to combat any peritoneal infection. Decompression, or at any rate the prevention of further distension, is achieved by continuous suction from the stomach or from the intestine. Though suction from

the intestine is theoretically superior, in practice continuous gastric suction seems [illegible]

duodenum and thence into the jejunum, this manœuvre becomes much more [illegible]

into the duodenum, but frequently the attempt fails When the tube has entered the duodenum, the balloon is inflated to stimulate propulsion and continuous suction is started. The suction must be accompanied by replacement of the fluids aspirated by equivalent amounts of water and electrolytes, and this will mean parenteral infusion (p 96) It should be realized that fluid lying in distended intestinal loops is lost to the circulation as surely as if it had been vomited. The fluid balance chart, which must always be kept, inevitably includes this source of error The repair solutions to be used are detailed on pp 103-111. [illegible] important the [illegible] days or even [illegible] staff to be rew[illegible] details of water and electrolyte balance and parenteral feeding. If the case is due to a subacute mechanical obstruction, for example, as in Crohn's disease in which conservative management is to be tried, and there is much colicky pain, antispasmodics should be given to relieve it. Atropine seems as effective as any of the newer synthetic drugs, and 1 mg should be injected intravenously very slowly The borborygmi may be hushed and the pain may subside before the injection is concluded This dose of atropine given subcutaneously will need repetition hourly or two-hourly In the case of paralysis of the bowel from [illegible]

made to stimulate its activity In post-operative ileus which is unassociated [illegible]

and fluid and electrolyte loss replaced, normal function will return in time. As [illegible]

and if the organisms causing the infection are not known, penicillin and streptomycin should be given empirically.

REGIONAL ENTERITIS

Crohn's Disease

This term is applied to a non-specific, usually chronic, inflammatory lesion found in one or more areas in the small or large intestine. Typically the bowel is thickened with a narrow lumen while the mucosal surface shows varying degrees of ulceration. The mesentery is thickened and contains numbers of enlarged lymph glands. It is possible that a number of separate disease processes are at present included in this definition.

The patient may present in various ways. The first attack is frequently ... an attack of ... ire, the case ... present with ... of the malabsorption syndrome.

There is no known specific treatment. If the disease is of moderate or severe degree, the patient will have to be nursed in bed. It is important to persuade the patient to take as nutritive a diet as possible, and in view of the possible danger of obstruction it should be low in residue. Chemotherapy should not be given as a routine but reserved for more severe exacerbations, for preoperative preparation if surgery becomes necessary or for post-operative ... in the same dosages ... tion; the usual precautions for cortisone or corticotrophin therapy apply (p. 79). It is possible that those cases who present with the picture of acute inflammation, ulceration and bleeding respond best to this therapy. Pain is often a feature of regional enteritis. The severe exacerbations of colicky pain which are accompanied by borborygmi, easily heard on auscultation, are clearly due to obstruction. One mg. atropine intravenously will usually relieve them dramatically, and, if it does, the same dose can be injected subcutaneously as necessary, e.g. two-hourly, until the attack wears off. The attack of obstruction may persist with distension and vomiting, and a decision will then have to be taken whether to treat it conservatively or whether to operate. Usually the wisest course is to temporize and treat the condition conservatively using con- ...

Apart from these episodic pains, there is often a constant pain ... peritonitis. This will require analgesics, such as tab. codein co. or pethidine. For the anæmia, iron may be given or transfusion may be required. These measures may have to be continued for weeks as the disease waxes and wanes. Useful indices of the progress of the disease are furnished by the pulse and temperature chart, variations in the erythrocyte sedimentation rate and the ...

affected portion of the gut. At first sight resection promises a cure of the disease, but when patients are carefully followed up, it is found that a very

separate resections or a massive resection of the bowel. Such operations can be followed by an intractable state of malabsorption

MALABSORPTION SYNDROME

This name is given to a group of conditions in which the most prominent clinical feature is a defect in absorption of one or more foodstuffs The term foodstuffs includes water, vitamins and electrolytes. The absorption defect may be due to either organic or functional changes in the small intestine. For all practical purposes, the small intestine may be considered to be the only part of the gut through which foodstuffs enter the body, though very limited absorption can occur from the stomach and from the large intestine.

Malabsorption occurs when a large part of the small intestine has been resected, as, for example, for extensive mesenteric thrombosis It is also a

in which, as a result of some previous operation, there is a " blind loop " in the upper part of the small intestine. A " blind loop " exerts an extremely unfavourable effect on intestinal function, which is manifested as a defect in absorption that may be extremely severe

Organic disease of the small intestine may be responsible for the syndrome, as in regional enteritis or in a tuberculous enterocolitis, though the latter condition is now less common

There remains a group of diseases, namely cœliac disease in children (see p. 252) and tropical sprue and idiopathic steatorrhœa in adults (see pp 215, 216), in which malabsorption is the chief defect but which are said to have no structural abnormality in the intestine in the early stages.

In the syndrome there may be defective absorption of one or more elements of the diet. Since fat seems to present most difficulty in absorption, excess of fat in the stools is often a prominent feature, so that the condition used to be spoken of as " steatorrhœa ". This name should be abandoned. Research indicates that in a severe case all elements of the diet, even including electrolytes and water, are inadequately absorbed Failure to absorb nitrogenous products produces creatorrhœa and ultimately a hypoproteinæmia. The steatorrhœa may be so gross as to produce pale, bulky, greasy stools, obvious macroscopically, or may be so slight as to pass undetected until a fat balance test is done

Of the cation electrolytes, calcium presents the greatest difficulty in absorption, as it forms calcium salts with the free fatty acids in the intestine In addition, absorption of vitamin D may be defective If there has been long-

as if it is associated with a "blind loop" or with some intestinal fistula it may be *remedied surgically. It is most improbable that a "blind loop" will be detected* radiologically, and its presence can only be suspected from the history of a previous abdominal operation. The condition will only be discovered at laparotomy, and resection of the loop should be followed by complete recovery. Intestinal fistulas are also difficult to demonstrate radiologically and their closure is also followed by a return to normal health. Malabsorption due to tuberculous enteritis probably indicates irreversible change in the bowel, but in the active stage of infection the disease may be treated. Therapy is that of tuberculosis elsewhere in the body and is usually highly successful (see p. 122). *The duration of treatment will depend on the extent of the pulmonary infection* present. If this is minimal, treatment may be concluded in two to three months. If there is extensive pulmonary disease, treatment will have to continue for at least a year. While operation may be indicated for obstruction in cases of regional enteritis, there is no good evidence that resection of the affected gut improves absorption elsewhere, and the absorptive defect can only be treated on the symptomatic lines to be described Cœliac disease in children is now generally regarded as a malabsorption defect induced by gluten, a protein of wheat, and if this offending substance is excluded from the diet a striking improvement results The diet must be continued for many years, certainly throughout the growth period and possibly throughout life. Improvement shows itself in the ability of the child to absorb fats, to grow and to develop normally. Idiopathic steatorrhœa in adults can also be treated by this diet with good results in a high proportion of cases. It may, however, have to be continued for many weeks or even months before improvement is apparent. *Details*

the cause cannot be

prescribed is high in

protein with a fat intake restricted to 50 g. a day in the first instance. Certain fats seem better tolerated than others.

while meat fats present more difficulty.

length of fatty acid chain, but are not fu...

are given on p. 216. The clinical course of a case with the idiopathic malabsorp*tion syndrome* shows periods of remission and relapse, and rest in bed may help

calcium

its daily,

to give it

by injection. Treatment of a state of gross calcium deficiency *must* be prolonged

The anæmia so frequently

Folic acid in doses of

n the anæmia is mega-

and sore tongue If the mean corpuscular hæmoglobin concentration ... 28 per cent., iron is necessary, either by mouth as ferrous sulphate, 0.5 g. thrice daily, or, if this proves ineffective, by parenteral injection.

In certain cases cortisone or corticotrophin has an action in improving

absorption in the gut, but the effect seems temporary and inconstant. It may be tried if all else fails, but cannot be recommended as a routine treatment.

BACILLARY DYSENTERY (p. 16)

AMŒBIC DYSENTERY (p. 211)

CHRONIC IDIOPATHIC ULCERATIVE COLITIS

The term "idiopathic ulcerative colitis" is used to describe an inflammatory condition of the [illegible] which is not attributable to a [illegible] an acute or chronic course [illegible] the rectum [illegible]

and blood but no *E. histolytica*, and no specific dysenteric organisms can be cultured. Examination of the rectum endoscopically may show varying degrees of inflammation, and unless the condition is limited to the rectum, a barium enema will show changes in the colon.

General Management.—All grades of severity occur, from the mildest cases of proctitis in an ambulant patient who passes one or two loose stools a day and occasional blood, to a fulminating condition in which the evacuation of watery, bloody stools occurs ten to twenty times daily and which leads to death within a few weeks.

There is no specific treatment. If the symptomatic measures discussed below are provided and maintained, a partial or complete remission is likely in the majority of cases. These measures may have to be continued over long periods since the course of the disease extends over months or years rather than weeks.

Ulcerative colitis is a wasting disease, and the maintenance of nutrition is the chief consideration in treatment. Water and electrolyte loss must be replaced as outlined elsewhere. In the case of severe disease, the fluid loss may be quite considerable, the stool volume measuring up to 2 litres a day. The loss of [illegible]

of protein through the bowel may reach a value of more than 50 g. a day, and losses of this order may continue for some weeks. In addition to this direct loss [illegible]

exception of extensive burns, in which, though the loss may be even higher, it is not so prolonged. This loss of protein naturally presents a profoundly difficult

therapeutic problem, as the patient with a fulminating attack finds it difficult

the milk can be fortified with Complan, which is a dried-milk mixture with the addition of fat, sugar, *mineral salts and vitamins. Some patients will prefer* Complan made up with water, and this mixture comprises a sufficient food in itself. It is not possible to prescribe these foodstuffs rigidly, as each patient

made good by the parenteral infusion of plasma in amounts of a litre or more daily Another method of maintaining nitrogen intake is by the use of protein hydrolysates (p. 710) If these measures of nitrogen replacement are to be carried out rationally, a nitrogen balance chart should be kept, the total losses and the total intake being recorded. Though the clinical picture of acute fulminating ulcerative colitis is very dramatic, it is fortunately uncommon Most

ferrous sulphate, 0 2 g. (3 gr.) thrice daily, will be sufficient.

Cortisone.—The use of cortisone or corticotrophin greatly increases the chance of a remission, particularly in the first attack. It is not yet certain which of these is preferable. Cortisone or corticotrophin should be given to all cases

his depression and becomes cheerful and even optimistic. It increases appetite so that the patient may sometimes say that he is unable to take enough food to produce the feeling of satiety. It is possible it also acts on the colon directly by reducing exudation and therefore the loss of protein through the bowel mucosa. All these actions are of value. The objections to its use are few. There may *be some retention of sodium and water, but there is no need for concern over* slight œdema. To combat the increased potassium loss it is usual to give potassium salts, such as potassium chloride, 2 g (30 gr.) four times daily. It is always necessary to bear in mind the risk of giving cortisone to a patient with a tuberculous lesion or a past history of peptic ulcer. If corticotrophin is given, the dose should be 80 units of the gel by intramuscular injection daily, and if no remission is obtained the dose may be increased to 120 units a day. Sodium retention seems to occur more frequently than with cortisone and may have to be treated with mersalyl injections, 1 to 2 ml. daily, and/or a low sodium diet. Potassium salts should be given as with cortisone. Treatment with these drugs should be continued until a remission occurs, *which is usually the case within six* weeks. The drug may then be withdrawn in the hope that the remission will persist. Sometimes the patient relapses on withdrawal of the drug, and treat-

If relapse again follows withdrawal, surgery

, the patient has to continue with some

plete remission.

Analgesics.—Pain is not usually an important feature in ulcerative colitis, though there may be pain with a bowel action The opiates are frequently prescribed, tinct. opii, 0·6 to 1·5 ml. (10 to 25 min), or pethidine, 100 mg., but in a disease with such a prolonged course the risk of addiction must be

treatment.

Psychological Treatment.—The psychological state of the patient with

to ulcerative colitis. It is seen in any patient who has experienced chronic diarrhœa for weeks or months from whatever cause and has lost 10, 20 or even 30 per cent of his body-weight. It seems that no ordinary human being can remain calm, cheerful and equable under the conditions imposed by ulcerative colitis, and this state should therefore be regarded as a normal response to these conditions Whatever the original personality may be before the onset of the disease, there is no doubt that a great part of the abnormality that is observed is due to the disease and improves with amelioration of the colitis. The most

where this atmosphere exists or in a unit where special interest is taken in patients with this disease. There is no indication for any formal psychotherapy

dications for

There is as

ays a part in

promoting a remission or preventing a relapse

Assessment of the course of the disease is aided by a record of the pulse, the temperature and the E S R. The number of stools passed daily or their total volume can usefully be charted, the patient should be weighed regularly If

the stools

the patient

scopic and

radiological examination, though these are contra-indicated in the severely ill patient.

Complications.—There are various complications of ulcerative colitis, such as perforation, hæmorrhage, fistula, polyposis, stricture and malignant change, which affect the colon. There are also other complications elsewhere, such as skin conditions, arthritis, iritis and iridocyclitis, endocarditis and nephritis These conditions may be expected to heal or improve when the colitis subsides, but their presence may influence the physician to consider radical surgical therapy

Surgery.—The medical management of ulcerative colitis has greatly

condition of the patient can usually be so greatly improved prior to operation that, in the best hands, total colectomy carries only a minimal mortality, less than 5 per cent. The decision to make a permanent ileostomy, however, particularly in a young girl, is one which should not be lightly undertaken. A patient may be considered suitable for surgery because of the intractability of the disease, that is, because of repeated relapses despite adequate treatment, or because of certain complications, e g. colonic or rectal stricture or rectovaginal fistula. If surgery is indicated, the operation and its consequences must be frankly discussed with the patient. It is helpful to get someone who has had a successful colectomy and ileostomy to discuss the matter privately with the patient before he reaches any decision. On no account should anyone be per-

a patient who has been having cortisone therapy. The danger of depressing the function of the adrenal gland from prolonged administration of cortisone is discussed elsewhere (p 83) When the patient on cortisone is in remission, the

hydrocortisone. The administration of corticotrophin is then discontinued and a test of adrenal function carried out If the response is satisfactory, it is safe to proceed with the operation. Cortisone can be held in reserve should definite symptoms of hypoadrenalism appear post-operatively.

The patient with an ileostomy will find out by experience any special foodstuffs which seem to stimulate the ileum and thus learns to avoid them The iliac contents can be thickened if the patient ingests one of the synthetic preparations of methylcellulose, e.g Celevac. A patient with an ileostomy should not be discharged from hospital without being warned that, if the ileostomy ceases to function, he should immediately inform his doctor. Stoppage of an ileostomy is usually only temporary, and it can sometimes be rapidly relieved by passing a catheter through the ileostomy opening. If the obstruction persists, the patient should be treated as for an intestinal obstruction.

DIVERTICULOSIS : DIVERTICULITIS

Diverticula may occur anywhere in the gastro-intestinal tract, but are most commonly found in the colon They may be found on routine barium enema examination in something like 10 per cent. of patients examined over the age of fifty. The existence of such diverticula is spoken of as diverticulosis, while if inflammation occurs the term used is diverticulitis. The mere existence of diverticula is therefore considered by definition to produce no symptoms. The symptoms of diverticulitis are those of discomfort or pain in the left iliac fossa, with periods of constipation and possibly diarrhœa. Some local tenderness may be noticed. If the condition progresses with the occurrence of repeated attacks,

the patient may present with colonic obstruction. Occasionally the onset is heralded by a massive hæmorrhage. The diagnosis is made on the history, the finding of a palpable, thickened, tender colon in the left iliac fossa and by a barium enema examination. Endoscopic examination will exclude most other lesions; it is frequently difficult to rule out a carcinoma of the bowel. This may be impossible on radiological examination, and difficult even when the bowel is examined at operation.

If diverticulosis is discovered accidentally at radiological examination, it may be wisest to say nothing about it to the patient. If diverticulitis is giving rise to mild symptoms such as periodic constipation and discomfort, the patient may remain well by avoiding excessive roughage in his diet and taking paraffin as a regular aperient—15 ml (1 tablespoonful) thrice daily. An exacerbation, as indicated by the occurrence of fever, pain in the left iliac fossa with some tenderness and a little distension, and constipation perhaps alternating with diarrhœa, should be treated more seriously. The patient should go to bed and take a low-residue diet. Heat is effective in relieving pain and may be applied by short-wave diathermy if available or an electric pad. Analgesics such as tab. codein co or pethidine may be necessary. If there is fever, leucocytosis and a raised E S R, chemotherapy is clearly indicated. Since the infecting organism will not be known, the combination of procaine benzyl penicillin, 300,000 units daily, with streptomycin, 0 5 g twice daily, should be given. The course may last from seven to ten days, depending on the response obtained. The inflammation may take some weeks to resolve. If obstruction is present with other signs of inflammation, a colostomy may be necessary. Resection of the affected portion is, however, the treatment of choice. In the past, when operations on the colon of the elderly patient were attended by much risk, this procedure was rarely considered. Due to better anæsthesia, an improved knowledge of water and electrolyte balance, the use of blood transfusion and the help of chemotherapy, it is now possible to undertake radical resection in many subjects. Surgical treatment will also have to be considered in cases with severe bleeding. Laparotomy is also indicated where the diagnosis is in doubt and the possibility of carcinoma exists.

CONSTIPATION

Constipation may be defined as an infrequent evacuation of fæces, but what constitutes "infrequency" differs considerably from subject to subject. Some people regularly have a bowel movement two or three times a day, while others are content with an action once in every two or three days. Constipation has been classified into colonic constipation and dyschezia or rectal constipation. The latter is more common, and indeed may be the only type. The causes of constipation are various, but probably the most important is the neglect of the impulse to defæcate and the consequent failure to develop a regular bowel habit. Children should be trained as unemotionally as possible to obey the call to defæcation. Over-training by an anxious mother can be harmful in making the child unduly bowel conscious. Another factor may be the sitting posture usually adopted in Western countries, which is not as effective as the more natural squatting position used in other parts of the world. One cause of constipation is undoubtedly the widespread use of laxatives encouraged by certain manufacturers. By over-emphasizing the mythical dangers of a failure to obtain a daily action, the subject is prevented from developing a natural bowel habit. In many

homes a ritual purgation is carried out once a week, which is inevitably followed by a period of constipation to allow the colon to fill up once more. Weakness of the various voluntary muscles taking part in the act of defæcation may be of importance in the causation of constipation in elderly persons and following pregnancy.

It is important in the first instance to be quite certain that constipation is actually present. A patient on a low caloric diet or one with little residue cannot expect his bowels to open oftener than once every two or three days. Since constipation inevitably follows purgation, it may be necessary to forbid the use of all purgatives before deciding that treatment is in fact required. In the elderly patient, or in a woman after pregnancy, it is worth trying to improve the musculature by suitable exercises. Since the normal stimulus to movement of the bowel is distension of the gut, a diet with a high fibre or roughage content producing a bulkier stool will tend to relieve constipation. Green vegetables, parsnips and peas, wholemeal bread and bread made from high extraction flour are valuable sources of roughage.

It is possible that constipation may be caused by a "greedy colon" which abstracts too much water from the colonic contents. The resulting fæces fail to stimulate their expulsion from the bowel. This explanation may be correct, but it seems doubtful if encouraging the patient to drink more fluid will help the condition, though this is the advice commonly given. Mild constipation should be treated by stopping the use of all drastic purgatives, by giving advice about a suitable diet, and by explaining in simple language the causal factors leading to constipation. These measures may, however, be insufficient and it may be necessary to use some additional aid, particularly during the period in which the bowel habit is being regained For this purpose the least harmful measures are those which stimulate the bowel by increasing the bulk of the stool. There are two groups of these substances used for this purpose, namely the saline aperients and the hydrophilic colloids. All the saline aperients have the common property of containing an ion which is not readily absorbed. They, therefore, tend to retain water, or by osmosis to attract water from the gut wall, until the solution within the bowel is isotonic with the body fluids. This increase in fluid bulk provides the stimulus to movement of the bowel. The salts which are commonly used fc [illegible] sodium
sulphate, 5 to 15 g,
tartrate, 10 to 15 g.
choose between them on pharmacological grounds, but some of the preparations are pleasanter to take than others, e.g. effervescing sodium phosphate, 8 to 16 g

The hydrophilic colloids are substances which, in the presence of water, swell up to form a colloid solution, thereby increasing the bulk of the fæces. The most commonly used is agar, a substance obtained from seaweed The dose is 8 to 16 g. and the dried material may be sprinkled on moist food such as stewed fruit. It is also given emulsified with paraffin in a dose of 15 to 30 ml. of emulsion. The dried seeds of various tropical plants contain gums with this hydrophilic property, and Isogel is an elegant proprietary preparation of this kind Since they imitate the natural action of roughage, there are no drawbacks to their use, though it is possible, if excessive doses are given, to produce intestinal obstruction. Such incidents have been reported and are analogous to obstruction produced from eating masses of fibrous foods such as tough grape-fruit or oranges.

As an aperient, paraffin is a widely used substance which softens the fæces and possesses a lubricating action. It is best taken in doses of a dessertspoonful after meals to ensure that it mixes evenly with the food. There is good evidence that paraffin is absorbed from the intestine in small amounts and may provoke a foreign body reaction in the intestinal mucosa, the mesenteric lymph nodes or the liver. It can also be shown to reduce the absorption of fat-soluble substances, notably carotene. Large numbers of people, however, take paraffin habitually with no apparent ill effects. Paraffin is often given with other substances, e.g. as an emulsion with magnesium hydroxide, or with agar, or with agar and phenolphthalein.

Lastly, there is a large group of irritant cathartics which have been widely used for many centuries and which depend for their action on irritation of the [illegible]

Enemata are used to empty the lower bowel. By virtue of the bulk of introduced fluid, bowel movement is stimulated. They should not be used routinely for the treatment of constipation. If the fæces are hard and inspissated, the prior introduction of olive oil into the rectum may be of value. The use of wetting agents, e.g. 1 per cent. dioctyl sodium sulphosuccinate 2 ml. orally to allow penetration of the fæces by water has been recommended and the reports of their use are encouraging. In the constipation of myxœdema, thyroid extract is extremely effective. Bile salts have an aperient action and may be indicated in the constipation of obstructive jaundice. Impaction of fæces, as occasionally occurs in the elderly, may [illegible] may even be necessary [illegible] occasionally have to be cc [illegible] cure. Though radical surgery is rarely required for the management of constipation, in carefully selected cases it can be extremely effective and its results welcomed gratefully by the patient. With pre-operative sterilization of the bowel, and in an otherwise healthy patient, the operation carries little risk.

PARENTERAL FEEDING

In various diseases of the alimentary tract or after operations on the stomach or intestine, normal feeding may become difficult. Examples that may be cited are obstructions of various sorts, e.g. pyloric obstruction, paralytic ileus following an operation, or temporary obstruction in Crohn's disease. In fulminating ulcerative colitis it is essential to tide the patient over a period of severe malnutrition until a remission is obtained. In all such cases nutrients may have to

be introduced parenterally. It is possible to maintain a patient's nutrition for many weeks with parenteral feeding.

The requirements of the patient may be considered under two headings—calories and protein.

Calories.—When oral feeding is possible, the caloric needs of the body are met by the ingestion of a variety of foods containing carbohydrate, fat and protein. It is not, of course, practicable to introduce all these substances parenterally.

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be circumvented by giving glucose in 20 to 40 per cent. solution by catheter introduced via the median basilic vein into the superior vena cava. In order to minimize any clotting tendency, 1 unit of heparin may be added to each ml. of the infusing solution If the glucose is introduced faster than the body can utilize it, glycosuria will result. It is said that fructose (lævulose) is utilized more rapidly than glucose, and a 10 per cent. solution of invert sugar which contains a mixture of equal parts of glucose and fructose has therefore been recommended for intravenous use

Fat is a concentrated source of calories, since it yields 9 Cals per gramme. It has been used intravenously with success in 15 per cent. emulsions, but there is some difficulty in preparing a stable emulsion, and at the time of writing there is no suitable preparation available in Great Britain.

Alcohol is of great ... Cals. The maximum rate of inf ... 56 Cals or 1,300 Cals. in the twe ... l appears to proceed independently of the metabolism of other constituents so that it may be given together with glucose. If this dose is not exceeded, no symptoms are evident beyond a little flushing or drowsiness Alcohol is thus useful in helping to maintain an adequate caloric intake. If glucose or alcohol is given for longer than a day or two, it is wise to ensure that the patient receives sufficient of the vitamin B complex. An ampoule containing a mixture of thiamin 5 mg., ... pyridoxine 2 mg. and pantothenic acid

... glucose can, at any rate in the healthy ... of protein, nothing can take the unique place of protein in the body, and it can only be replaced by protein, *polypeptides* or amino acids The only protein that is used for infusion into the human body is human plasma, and this may carry the virus of infective hepatitis. Not- ... It acts by raising the

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protein, mainly in the form of amino acids, which can be given intravenously. These are given in a 5 per cent. solution and in the protein depleted patient are said to be utilized even more rapidly than a 5 per cent. solution of glucose. There is no doubt that in normal man nitrogen balance can be maintained by the intravenous infusion of protein hydrolysates. If given too rapidly, as with glucose, some amino acids may appear in the urine, occasionally reactions from the infusion occur. It is necessary to emphasize the word " normal ", as in certain " stress " conditions, such as follow major operations, or with severe infections, the body is in a state in which infused nitrogen cannot be utilized, and at these times infusions of amino acids serve little purpose. It therefore follows that the parenteral feeding of amino acids will be of the greatest value when there is some mechanical difficulty to the ingestion or some failure in the absorption of oral protein, rather than when a metabolic difficulty is present during certain phases of " stress " It is necessary to give with the nitrogen a sufficiency of calories to " spare " the nitrogen for protein anabolism The aim should be to give 100 to 200 Cals. for every gramme of nitrogen infused. After an extensive resection of the gut for a mesenteric thrombosis, the nutrition of a patient can be maintained by parenteral feeding until the remaining part of the gut assumes its new function To summarize, plasma infusions should be given intravenously where it is desired to replace rapidly protein depletion Maintenance feeding of a patient may be carried out by infusing a solution of 5 per cent glucose, 5 per cent amino acids and 5 per cent alcohol at the rate of 100 to 120 ml an hour, giving 2 5 to 3 0 litres in the twenty-four hours This feeding is approximately 120 to 140 g. protein and 2,220 to 2,800 Cals daily, of which total some 90 per cent should be utilized by the body

PERITONITIS

The peritoneum is affected by acute and chronic infections and by malignant disease most commonly secondary to growths elsewhere

Peritonitis due to acute infection is either primary or secondary. Primary peritonitis, which is very rare, occurs more often in children in association with an infection, either streptococcal or pneumococcal, arising elsewhere in the body. The diagnosis of primary peritonitis may be difficult and the condition may only be recognized when, at laparotomy, no intra-abdominal cause for it is found. This form of peritonitis usually responds well to appropriate antibiotic therapy

Secondary peritonitis is commonly due to perforation of an ulcer of the stomach or duodenum, to perforation of an inflamed appendix, to spread of infection from an infected gall-bladder or from diverticulitis. It may develop after an operation on the bowel. Particularly dangerous is the biliary peritonitis which may follow rupture of a gall-bladder.

Prevention.—Many cases of perforation of the appendix still occur following the administration of castor oil or other purgatives to children with abdominal pain not recognized as being due to appendicitis. This mistake should not be made Perforation can be prevented by early diagnosis and operation Perforation of a peptic ulcer is also to some extent preventable. If a ... to have an ulcer develops an acute exacerbation ... tenderness and rigidity h... to subside An acut·

dyspepsia is not preventable, but such perforations are less serious and show a strong tendency to close spontaneously.

Treatment.—If secondary peritonitis from whatever cause is diagnosed,

carried out; water and electrolyte balance must be maintained by parenteral *infusion*.

Chronic peritonitis is usually due to tuberculous infection, though the condition is now relatively rare due to a steady decline in the incidence of tuberculosis. It is attended by loss of weight and the presence of ascites and fever, while enlarged glands and matted bowel may be felt on palpation. *Frequently the condition is only diagnosed when it is encountered at laparotomy.* It responds well to treatment in a sanatorium together with anti-tuberculous drugs, such as a combination of streptomycin 1 g. three times a week and para-aminosalicylic acid 12 g. daily.

FUNCTIONAL DISEASE

One of the most obvious and important characteristics of a living object is its perpetual adjustment to a continually altering situation, a process of adjustment which profits by past experience. Many mechanisms in the body may be thought of as perpetually attempting to bring the body once more into equilibrium after this has been disturbed Such mechanisms are called homeostatic.

If this phenomenon is accepted as a fundamental characteristic of living matter, it may be said that disease occurs when this power of adaptation breaks down. Complete failure of response may result in death of the individual, but failure short of this may produce what we call organic disease, or functional disease in the sense of a functional derangement of an organ, or both

Experience derived from large numbers of men who were subjected to severe stresses of war suggested that no person is completely immune to breakdown. When this results from trivial stresses, however, it is an indication of a poor or inadequate personality.

The pathways of communication along which the effects of stress can operate are nervous and hormonal If emotion generated by a stress is not externally discharged, it may, so to speak, erupt into the involuntary nervous system and in so doing affect profoundly the homeostatic mechanisms of the body Since the gastro-intestinal tract is richly supplied with autonomic nerves, it is not surprising that it is frequently affected by an emotional situation. It is now recognized that the effects of stress can also operate through a hormonal pathway producing in this way more prolonged effects. An example of this is hæmorrhage or perforation of an ulcer occurring within a week or ten days of some severe stress. There is considerable evidence that such peptic ulceration is associated with the secretion of excessive amounts of corticoids which are also known to augment gastric secretion. Such ulceration must be classified as organic because of its structural changes, though its onset may be closely related to emotional stress. Once a particular situation produces an abnormal bodily response such as diarrhœa, the same situation tends to reproduce it on each occasion, as if some kind of facilitation process existed. Organic and functional disease frequently

exist together, and their separation may prove extremely difficult. Organic disease, if sufficiently severe, may provoke an abnormal psychological response. Extreme loss of weight, for instance, is always accompanied by some changes of personality, such as depression, apathy or even suicidal tendencies, changes which disappear if the patient regains his original weight.

The relation of symptoms to some emotional situation do... mean the symptoms are solely functional... spasm of the lower... If, however, th... ly from peptic œs... e severe dysphag... Similarly, ... spasm induced by emotion ... such as results solely functional in origin, since inflammation of the colon may also be present. Errors of diagnosis are particularly liable to be made when symptoms have a double origin diarrhœa occurring from emotion will produce... is not necessarily

The taking of a full history in the case of functional disease is not only an essential diagnostic procedure but also carries considerable therapeutic value. It has been recognized for centuries that the expression of emotion to a neutral recipient seems to act as a beneficial catharsis A complete history of the situation and an assessment of the patient's personality can only be obtained gradually and may require more than one interview. The personality is judged by the adjustment the patient has made to his family, his work, the community, the opposite sex, to parenthood and in fact to all that constitutes his environment After completing the taking of the history, a careful physical examination should be made supplemented by radiological and laboratory examinations where these are indicated. These examinations are undertaken not only to satisfy the doctor but are also necessary to gain the confidence of the patient and to provide a rapport without which it is impossible for a doctor to exert his full influence.

When a diagnosis of functional disease is made, it is frequently necessary to give the patient some explanation of his symptoms and the way in which emotion can affect bodily function This explanation is often of great therapeutic benefit to the patient. It has so far been assumed that the patient is able to achieve some insight into his condition and to make some move towards reorientation There are, however, individuals with a general constitutional inadequacy who give a history of recurrent indefinite complaints, who lack insight and determination and in whom treatment rarely leads to good results It is important for the doctor to recognize such patients

Drug therapy may be of some value, e g. codeine in nervous diarrhœa, in which it is nearly always effective. The use of such a drug gives the patient confidence so that the habit of nervous diarrhœa, which may have become a conditioned reflex, is broken If, however, there is no obvious reason for prescribing a drug, the situation producing the abnormal response can only be affected either by altering the patient's personality or by altering the situation responsible Though some alteration of the patient's personality is generally possible, it becomes progressively less easy to achieve with advancing age. Altering the environment is a less heroic solution but one which may be very effective in circumstances where the situation is primarily at fault, e.g where a patient is obviously a misfit at his work.

Improvement of the physical condition of the patient should never be neglected. All patients with loss of weight from malnutrition or from

malabsorption will inevitably show abnormal emotional reactions; all patients suffering from prolonged pain will similarly show some form of abnormal response. Continued lack of sleep has an equally deleterious effect. The gain of a stone or two in weight from rest and a high caloric diet is a type of therapy, first popularized by Weir Mitchell, which deserves revival.

Finally, if no means can be found of strengthening the patient's personality, if the environment cannot be altered, and if drugs and physical measures are ineffective, the patient must accept his disability as inevitable.

SPECIAL SYNDROMES

Anorexia Nervosa.—If loss of appetite is severe in degree and is conditioned

and not in the patient's own home. The psychological difficulties that occasioned the anorexia may be quite superficial and readily removable by the family doctor, or the disorder may lie more deeply and require treatment by a psychiatrist.

ust insist that the

what it feeds on

and attractively

served. A nurse should be present at mealtimes to ensure that the patient does

apparent cure are common and are usually precipitated by some emotional difficulty.

Nervous Dyspepsia.—This term is used to describe a condition in which

ments and the secretory activity of the gastro-intestinal tract and the blood flow to it, and hence it seems likely that some altered pattern of behaviour is responsible for these symptoms. Nervous dyspepsia is usually suspected from the history and from the way in which it is recounted, the symptoms being frequently dramatized After organic disease has been excluded by appropriate examinations, the patient should be reassured and told that his symptoms, while perfectly genuine, are due to excessive activity or irritability of his stomach. He should then be treated on the general lines described above. Frequently such patients recognize that they have a "weak stomach" which takes the brunt of any fresh stress, but they desire reassurance from time to time. If they have some special diet to which they attach great importance, it should not be altered.

Psychogenic vomiting.—This type of vomiting occurs in the morning

by eating later in the day

Glossodynia.—Not infrequently patients complain of a painful tongue

to have a deep-seated origin so that the complaint may almost amount to a delusion Its removal is difficult or impossible and the patient can only be encouraged to accept the disability as something genuine but not completely disabling or dangerous. Consultation with a psychiatrist may be advisable.

Irritable Colon.—This name is used to describe complaints originating in the colon and characterized by discomfort or pain, the passage of scybalous stools or, more rarely, by the passage of large amounts of mucus. The condition in a mild form is extremely common. Occasionally the attacks may be clearly related to some emotional situation though usually the precipitating incidents are unrecognized Attacks tend to be more frequent when the patient is subject to overwork or is suffering from insomnia The antispasmodic action of atropine may be of therapeutic value and the tincture of belladonna may be given starting with 2 ml. (30 min) or the substitutes for the belladonna alkaloids may be tried (p 482) Where the attacks follow a period of tension accompanied by insomnia, the timely use of a hypnotic may prevent them Attention to the mode of life may prevent some of the attacks. The condition, however, is one that is liable to be present throughout life and becomes manifest following crises of one kind or another

Nervous Diarrhœa.—This condition, from which most people have probably suffered at one time or another, is characterized by the passage of loose stools after meals or in response to some emotional situation. In severe cases visits to a theatre or travel in a train without ready access to a toilet become impossible Apart from the general therapeutic methods discussed above, the

DISEASES OF THE LIVER

HEPATIC FAILURE

A number of diseases of the liver, including acute viral hepatitis, chronic cirrhosis, and disorders due to biliary infections, may show similar manifestations of hepatic failure during their course It is therefore convenient to consider the treatment of those features in the first instance before proceeding to discuss the various hepatic diseases.

Jaundice, an increase of bile pigment in the tissues, is a common though not invariable concomitant of liver disease It is usually associated with other conditions such as obstruction to bile flow, or to a hæmolytic process, and it is these conditions, rather than the jaundice itself, which will demand treatment.

be prevented by giving intramuscular calciferol, 300,000 units monthly, and oral calcium gluconate, 15 g. daily Vitamin A is also poorly absorbed in these circumstances and 100,000 units should be given monthly by intramuscular injection to any patient with jaundice of more than two or three months'

duration. Fat absorption may be increased by giving bile salts, such as desiccated whole bile Desibyl, 0 6 g. thrice daily. Bile salt therapy is also indicated in the treatment of biliary fistula or where long-continued biliary drainage is being carried out

[illegible] ion should [illegible] effective, [illegible] Methyl- [illegible] given sub- [illegible] the dose should be reduced to the minimum necessary to prevent recurrence. Since the symptom is always associated with an obstructive jaundice, the cause should be removed if this is possible. If this is not possible and the obstruction is extrinsic in situation a palliative cholecystenterostomy may be performed.

Fœtor Hepaticus.—In terminal liver failure, certain volatile substances may escape detoxication by the liver and appear in the breath. There is no specific treatment known for this symptom other than the general management of hepatic failure. The odour may be sufficiently obnoxious to necessitate [illegible]

[illegible]

realized that a variety of neurological and mental features may occur during the course of liver disease which do not necessarily indicate impending death. Complete recovery is possible. The precise relationship between hepatic failure and the central nervous system is obscure. There seems no doubt, in view of the rapidity of the onset of symptoms and the equal rapidity of their disappearance, that the cause is biochemical. Experiments in dogs have shown *that if the portal blood is shunted directly into the vena cava, feeding the dog* on a meat diet will produce an " encephalitis " and the dog may lapse into coma. It has, therefore, been suggested that in human beings suffering from cirrhosis collateral blood channels bypassing the liver permit substances derived from [illegible]

into the systemic circulation of toxic nitrogenous products. There is no doubt that mental symptoms and even coma may be precipitated in patients with severe liver disease by giving a high protein diet or ammonium chloride as a diuretic. Hepatic coma may also follow surgical operation or may be precipitated by a large hæmorrhage, perhaps due to a reduction in the circulation of blood through the liver.

Treatment.—The administration of ammonium chloride or any other ammonium salt should be stopped. Any blood loss should be replaced by transfusion, and water and electrolyte equilibrium must be maintained. This will usually necessitate parenteral therapy. In addition, glucose should be infused intravenously in 5 per cent solution, or it may be given in 20 per cent. or higher strength if a catheter is passed into the vena cava. No protein should be given by mouth. If, as seems possible, infused protein may be utilized without unduly raising the amino acid content of the blood, then it becomes safe to maintain nitrogen equilibrium in these patients with plasma infusions. Certainly a patient can recover from hepatic coma while having plasma infusions, but there is as yet no proof that such recovery is expedited by

these means In addition an oral antibiotic, e.g tetracycline, 1 g six-hourly, should be given to sterilize the alimentary tract and prevent the formation of toxic nitrogenous substances by bacteria. If coma is associated with an obstructive jaundice and cholangitis due to calculus, there should be no hesitation in advising operation, however desperate the condition of the patient if the obstructive jaundice may be relieved Recovery from coma in such cases may be dramatic.

ASCITES

Ascites is a common occurren [illegible] it is frequently associated with [illegible] capillary pressure, and also a [illegible] osmotic pressure of the blood These two factors, however, are insufficient to explain completely either the ascites or the œdema of liver failure Formerly it was the custom to treat ascites only by paracentesis whenever the abdomen was uncomfortably distended It is now recognized that this procedure has the [illegible] further the patient's stores of protein If [illegible]

[illegible] some cases appears to have a beneficial effect in promoting a diuresis. Ion exchange resins are relatively ineffective and are not generally recommended.

PORTAL HYPERTENSION

This condition results from a variety of lesions which obstruct the portal circulation. In three-quarters of the cases the obstruction is in the liver (e g. cirrhosis), while in the remainder it occurs in the portal vein or the splenic vein. An understanding of these anatomical and pathological facts is necessary for correct treatment. As a result of the obstruction, anastomoses develop between the portal and systemic venous systems. Accordingly, one of the signs of portal hypertension is enlargement of the veins at the lower end of the œsophagus and in the fundal part of the stomach These varices are liable to bleed, and this constitutes the chief danger of the condition. As with other causes of severe hæmorrhage, transfusion of blood will be required It is possible to compress the site of bleeding of the œsophageal varices with a special instrument whose use has been developed in the United States, where cirrhosis of the liver is a more common disease than in this country. The instrument consists of a tube which has three lumens which connect respectively with a balloon in the stomach, [illegible] survive Those with poor liver function who go into coma tend to succumb.

streptomycin should be given to control the infection, and if these antibiotics are not successful repeated short courses of a wide spectrum antibiotic, such as tetracycline, should be given. Symptomatic treatment for the various manifestations of hepatic disease as described on pp. 507-511 will also be required.

DISEASES OF THE PANCREAS

PANCREATITIS

The cause of acute pancreatitis is still obscure, but the simplest view is to regard the inflammatory changes that occur in the gland as being due primarily to the liberation of pancreatic enzymes. This liberation occurs when the gland is actively secreting and the duct, for some reason, is blocked. The secretory pressure of the pancreas is high and release of these enzymes damages the gland Depending on the secretory pressure and the completeness and duration of the obstruction, different degrees of pancreatitis will be produced ranging from a transient œdema which subsides completely, to the full-blown picture of hæmorrhage, necrosis, gangrene and sloughing with subsequent bacterial invasion Such severe inflammation is always accompanied by considerable shock If this view of the ætiology of pancreatitis is accepted, a rational plan of treatment can be prescribed

Acute Pancreatitis.—The pain produced is severe enough to necessitate the injection of 10 to 20 mg ($\frac{1}{8}$ to $\frac{1}{4}$ gr) of morphine, a dose which will probably have to be repeated The disadvantage of morphine is that it constricts the sphincter of Oddi, thus tending to raise the secretory pressure within the pancreas, a disadvantage which is also shared with pethidine and methadone An attempt should be made to counter this effect by giving injections of atropine in doses of 1 mg ($\frac{1}{60}$ gr.) subcutaneously. Glyceryl trinitrate, 0·5 mg , sucked under the tongue every half-hour is also useful for this purpose. If shock is present, it may require treatment by blood or plasma transfusion

It is clearly important to try and inhibit all pancreatic secretions as far as possible. Stimulation of the pancreas can only take place through the vagal nerve or through a hormonereleased from the small intestine. The vagal stimulus can be blocked by atropine, 1 mg., injected subcutaneously at two- to four-hourly intervals Other vagal paralysants have been recommended, but there is no evidence as yet that any of them are superior to atropine Since the release of the secretory hormones, secretin and pancreozymin, only occurs when food or acid enters the duodenum and jejunum, it is essential to prevent this by prohibiting all food by mouth and by keeping the stomach empty by continuous aspiration. The patient must, therefore, be fed parenterally. During the first three days only water and electrolytes to replace the aspirated fluid will be necessary. Of the electrolytes it is important to remember that a sharp drop may occur in the serum calcium owing to the large amounts of this ion neutralized by fatty acids liberated during the process of fat digestion in the peritoneal cavity. [illegible]

produce a hyperglycæmia in a patient with a damaged pancreas. Though the immediate cause of the inflammation of the pancreas is due to autodigestion, this may be followed by bacterial invasion ; penicillin and streptomycin should

therefore be given as prophylactics When the inflammatory process subsides, the biliary tract should be investigated radiologically. Acute pancreatitis is frequently associated with calculous cholecystitis, and cholecystectomy will therefore be indicated in many cases.

Subacute Pancreatitis.—This is a condition characterized by repeated attacks of pancreatic pain, though usually of less severity than that of an acute attack. It is likely that the cause of the pain is the same as in acute pancreatitis If the secretory pressure within the pancreas is moderate in degree, or the obstruction is incomplete, or the process is insufficiently prolonged, the severe degrees of inflammation seen in acute pancreatitis will not be produced in subacute pancreatitis In addition, pain is not usually accompanied by the same degree of shock. At this stage of the disease the destruction of the gland has not usually proceeded so far that secretion of juice is inadequate The therapeutic problem that faces the practitioner is not that of pancreatic insufficiency but [illegible] Such attacks of relapsing pancreatitis

king, some patients only get attacks

able to recognize the particular factor that precipitates an attack, he can obviously prevent its recurrence An attack of pain will require symptomatic treatment as already outlined. It will be necessary in every case to investigate the biliary system and, if there is a calculous cholecystitis, to recommend a cholecystectomy. In severe cases the operation of

pancreatic duct, and treatment has again to be directed towards relieving the attacks of pain. The choice may lie between bilateral splanchnicectomy, which cuts the pathways of pain to the spinal cord, and even a pancreatectomy.

Chronic Pancreatitis.—Chronic pancreatic insufficiency may develop following attacks of acute or subacute pancreatitis or without any previous history of the disease Such a case presents either with diarrhœa of unknown origin, usually fatty in type, or with malnutrition The differential diagnosis of this group of disorders, comprising the malabsorption syndrome (p 215), may present considerable difficulty, but tests for intestinal absorption of glucose, protein and fat, and estimations of pancreatic secretion will usually provide the correct answer. In cases of pancreatic deficiency it is possible to substitute pancreatin for the natural pancreatic secretion It should be given in doses of 4 g. before and after each meal Trypsin, the proteolytic ferment in pancreatin, is liable to be destroyed by acid and pepsin in its passage through the stomach. If the patient has achlorhydria, the trypsin escapes damage In such patients pancreatin taken regularly can achieve excellent results. If the stomach is

CARCINOMA OF THE PANCREAS

Carcinoma of the pancreas is not an uncommon form of cancer, and the disease may often present with obstructive jaundice or with an abdominal pain of unknown origin While a correct diagnosis can be made in most cases, it some-

times remains in doubt even at laparotomy. It is now possible to resect a carcinoma of the head of the pancreas together with the duodenum and to anastomose the bile duct, pancreatic duct and stomach to the first loop of the jejunum. A simpler palliative procedure is cholecystenterostomy to relieve the obstructive jaundice, and this is sometimes done as the first stage in the more radical operation. This palliative procedure is of great value in relieving the intolerable itching associated with the obstructive jaundice, and is justified as some patients with carcinoma of the pancreas live for one or more years after the diagnosis has been made at operation. Resection of the tail of the pancreas together with the sp
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W. I. CARD.

DISEASES OF THE HEART AND CIRCULATION

PRINCIPLES AND LIMITATIONS OF CARDIAC THERAPEUTICS

THE AXIOM that the first stage in rational therapeutics is accurate diagnosis applies with particular emphasis in diseases of the heart and circulation. Just as an adequate diagnosis may safeguard the patient from unnecessary restrictions and ill-chosen remedies, so it must be realized that, with few exceptions, complete restoration of function is not to be expected, even with the most energetic measures at our command. Certain defects, by their very nature, are no material handicap and call for no treatment, while for others it must be admitted that remedies, however desirable, are unfortunately unavailing. There is no more important factor in determining appropriate treatment than the ability accurately to assess the degree of circulatory incapacity existing at the moment. It is a well-known fact that many a patient may have definite myocardial or endocardial lesions with striking physical signs and yet be completely free of all symptoms during ordinary activity or even during sustained physical exertion. Of these patients it may be said that their functional capacity is good. They require no treatment for the heart itself, and indeed it is often a question if by any reference to the heart their attention should thus be directed to their circulation. At the other extreme there are those who suffer from all the signs of heart failure even at rest: their functional capacity is minimal, and for them every effort must be made to ease the cardiac burden and relieve their acute discomfort. The first step in treatment, therefore, is the assessment of the degree of circulatory impairment, and this is gauged by the ease with which one or more of the three major cardiac symptoms—pain, dyspnœa or congestion—is induced.

It is important to note that a physical sign in itself, particularly when regarded as the only manifestation of organic damage, seldom warrants active therapeutic measures. A systolic murmur, an irregular pulse, even an enlarged heart, while each demanding careful investigation before its nature can be accurately determined, are not in themselves to be regarded as indications for any particular treatment. It is well known that, in the past, many a patient with a perfectly sound heart has been rested unnecessarily for months at a time on account of an innocent systolic murmur, and all to no purpose. Similarly the waxing and

incapacity. There are exceptions to every rule, but it is a good principle which applies with particular emphasis in the therapeutics of heart disease—when the symptoms warrant attention, treat the patient and not his physical signs.

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at our disposal can only alleviate cardiac failure in so far as the myocardium is able to avail itself of the proffered help A time will surely arise when the futility of whipping the tired horse becomes more and more evident. Levine has pointed out that, for the most part, the best that can be accomplished by the intelligent care of chronic cardiac disease is a prolongation of life and relief from suffering, which year by year compares more and more favourably with the advantages obtained from the early diagnosis and treatment of malignant disease.

Priority goes to the restoration of "cardiac compensation", and in this the skilful use of drugs is essential. Nevertheless, in the prevention of relapses drug therapy is often less important than the patient's social and economic background · a dock labourer or a miner is clearly at a disadvantage as compared with a sedentary worker Measures calculated to reduce exertion and to avoid exposure and infection may rob a man of his job, and this usually means hardship for his dependants These circumstances tax the physician's judgment: the patient requires medical care, but an excessively academic approach to the problem may create havoc in the patient's household, and convert a case of minor valvular defect into a major cardiac neurosis

It is gratifying to record that the intensive study of heart disease during the past thirty years has been rewarded by great advances in its therapeutics, thus replacing the blind polypharmacy and inadequate care of the past. Further gains will be made when more of the ætiological factors responsible for the ultimate development of myocardial damage can be controlled or eradicated. Recognizing the limitations and encouraged by the possibility of aiding and guiding the recuperative powers of nature, it is with such broad principles as these that the physician approaches the treatment of heart disease.

VARIETIES OF HEART FAILURE

The heart fails when it is unable to supply the tissues with oxygen sufficient for their immediate needs The defect may first become manifest under conditions of strenuous exertion, later it accompanies moderate activity and finally it is continuously present even when the patient is at complete rest.

The type of failure which develops varies with circumstances, and hence a variety of clinical syndromes must be differentiated if appropriate measures for their treatment are to be arranged For example the syndrome of congestive heart failure, denoting the general inadequacy of the heart as a pump, demands measures which are in sharp contrast to those employed in the anginal syndrome or in the psychogenic disturbance commonly spoken of as the effort syndrome There are other varieties and subgroups to which reference will be made in appropriate sections.

THE SYNDROME OF CONGESTIVE FAILURE

Congestive heart failure is a clinical term for a syndrome difficult to define and difficult to measure. We can picture the young woman, the subject of rheumatic heart disease, handicapped by a massive œdema of the feet and legs, breathless to the point of orthopnœa, cyanosed, sleepless and exhausted Pleural effusions, moisture through the lung bases, portal congestion and diminution in urinary output, provide further evidence of the detrimental effects on the tissues of progressive failure of the heart as a pump This is an extreme example. In other patients in the earliest and mildest stages of failure, congestion may only

As a further principle it is reasonable to suppose that successful and appropriate treatment depends upon the removal or correction of the provoking cause of the cardiac distress. It must be admitted, however, that

this important cause of heart disease. With a greater proportion of the population

cardiac failure.

To live within the limits of his cardiac reserve—this is the golden rule to offer to the patient; and it is the doctor's business to explain what the rule implies. Ten hours in bed at night is a good investment against the exertion called for in a day's work, even though a couple of hours be spent in reading rather than in sleeping Some patients renew their strength by lying down for half an hour after the midday meal; others spend a whole day in bed once a week and thus stave off the symptoms of incipient cardiac failure. But gentle exercise is no less important than generous periods of rest: walking in the open

the doctor is not determined exclusively by purely professional skill. The general tenor of the physician's advice will be "Moderation in all things". The prevention of obesity is absolutely imperative. A change of occupation is often desirable. There are many reasons why this is frequently found to be impossible, but patients who are young and intelligent can sometimes be diverted to jobs which will not make excessive demands on their cardiac reserve even when the disease has progressed considerably.

There are few therapeutic procedures which yield more gratifying results than skilful drug therapy in the management of cardiac failure. The keynote of success is simplicity.

of a *limited number of*

the individual patient

pain, and the scope of dietetics.

With these broad principles in mind it is desirable to reflect on the limitations of active therapeutic measures. At the outset it will, of course, be realized that complete restoration of function is seldom to be expected, and for the most part structural defects in the muscle, valves and arteries are permanent and irremediable In consequence, a limit is set to what may be attained even by the best régime possible. This must not be permitted to prejudice or discourage the doctor in his endeavour to give adequate relief. The fact is that all the measures

at our disposal can only alleviate cardiac failure in so far as the myocardium is able to avail itself of the proffered help. A time will surely arise when the futility of whipping the tired horse becomes more and more evident. Levine has pointed out that, for the most part, the best that can be accomplished by the intelligent care of chronic cardiac disease is a prolongation of life and relief from suffering, which year by year compares more and more favourably with the advantages obtained from the early diagnosis and treatment of malignant disease.

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be evident in the prominence of the cervical veins, with œdema restricted to a few moist sounds at
towards evening
thorough treatm
minimal signs will show distinct improvement within a week or two of adequate rest.

It is clear that congestive failure tends to develop when the cardiac output remains inadequate for the needs of the tissues for a sufficiently long period. There is a time factor which influences the acuteness and the severity of the distress. It must be understood that the measurement of cardiac output is not in itself a measure of the degree of failure. Blood flow alters with change of posture, with variations in activity and with individual needs. For instance, a
severe anæmia has, even under basal
the heart fails in such a patient, as it
duced but may still exceed that of a

deficient only under conditions of sustained physical activity, but ultimately it

venous pressure with stasis of the blood in the veins and venous reservoirs emptying in the direction of the heart. As the venous pressure rises, congestion occurs with the development of transudates in the serous sacs and œdema of the organs. Compensatory arteriolar constriction leads to anoxia of the tissues with an increased blood volume.

is responsible for retention of water and sodium, and the reduction in flow to the muscles accounts for the feelings of fatigue and exhaustion—both common early features of congestive failure. Salt and water retention lead in turn to increased extracellular fluid, an augmented blood volume and an increase in venous pressure first apparent as a damming up of blood immediately behind the chamber of the heart primarily affected

Both theories are necessary to explain many of the effects observed. The forward-failure theory, emphasizing the role of the kidney, offers the best explanation for the formation of œdema, whereas the concept of backward-failure offers a ready explanation for the clinical picture of "congestion behind the lesion, anoxæmia in front". In acute failure of the left ventricle a sense of
is followed rapidly by urgent dyspnœa,
that the right side of the heart,
urn and passes on through the
pulmonary circuit a volume of blood which the left side is incompetent to

handle. The pressure in the pulmonary veins and arteries therefore rises with resulting exudation into the alveoli and the formation of a greater or less degree of pulmonary œdema. Much of the distress experienced by the patient depends on the rapidity of the reaction Similar mechanisms are responsible for right-sided failure.

Clinical Types.—Cases of congestive heart failure may be grouped for clinical purposes under various headings. As outlined above, there is a strong justification for the anatomical concept of left- and right-sided failure. In the former the dominant feature is an increased pulmonary blood volume, whereas in right-sided failure congestion of the systemic veins resulting in engorgement of the kidneys, liver, portal tract and subcutaneous tissues, is a common finding

Each variety occurs in an acute or chronic form Left-sided failure is commonly the result of aortic valvular disease, hypertension or myocardial infarction. Mitral stenosis can give rise to a similar picture before the right ventricle fails Right-sided failure may occur in chronic pulmonary disease, congenital heart disease, and particularly after long-continued left-sided failure. Simultaneous right- and left-sided failure is commonly found with hyperthyroidism, combined mitral and aortic valvular disease, severe anæmia, and when more than one ætiological factor is present, for example, emphysema with hypertension

veins engorged and the diastolic pressure higher than in the absence of failure. The inference is that in association with peripheral vasoconstriction the circulation as a whole is slowed and the cardiac output decreased.

High-output failure occurs when the primary fault is in the periphery and not

is met primarily by an augmented cardiac output. Under these circumstances a diminished peripheral resistance favours an increased blood flow, a speeding-up

low-output failure.

Finally, congestive failure may be classified on the basis of a disturbance in the rhythm of the heart. Thus groups may be differentiated as failure with normal rhythm, or failure with fibrillation, or again failure with paroxysmal tachycardia Such an arrangement is not without interest to the clinician; but it is too remote from basic physiological principles to provide more than an empirical approach to therapeutics.

Methods of Treatment.—The guiding principles regulating the treatment

f congestive heart failure are the provision of adequate rest for the heart muscle and the use of measures designed to increase its contractile efficiency

gents, (4) the use of diuretics, particularly the mercurial compounds.

Rest in Bed

At the outset it is wise to explain to the patient that absolute rest will be equired, and that this means remaining in bed for a number of weeks. Many

orced to retire to his bed with many business problems unsolved and domestic or ersonal difficulties still preying on his mind. It is often justifiable to permit uch a patient a couple of days to do what he can to put his affairs in order, so hat he may at once be rewarded by as complete a physical and mental rest as ossible.

vith

Everything must be done to render the patient as comfortable as possible by the rovision of a suitable number of pillows, support for the arms, a suitable mount of bedclothes and a warm but airy room Many a patient will beg to be llowed to sit in an arm-chair, saying that his breathing is thereby rendered more ree than when he is strictly confined to bed. As a general rule this reflects on he care which has been taken to give him the maximum amount of comfort vhen in bed If, on account of dyspnœa, the patient proves to be more comfortble sitting well supported in a chair, no harm is done by conceding to his equest. An hour or two out of bed each day reduces the risk of thrombombolic complications A support for the shoulders and a prop for the feet are evices which bring comfort, and when this is found, the correct position hould be maintained. The adjustable bedstead designed by Lewis for the ursing of cardiac patients has many advantages. By simple mechanical means he support for the back and shoulders is easily regulated to suit individual equirements By a similar device the feet and legs can be lowered so that a semiitting posture can be maintained with freedom from strain and with the maxinum amount of comfort.

For urination a bottle should be provided, but the patient may be pernitted to leave his bed for bowel actions, and for this purpose a bedside comnode should be provided. This concession cannot always be permitted, out it is useful to remember that many patients, particularly heavily built nd elderly men, expend much mental and physical energy in their unaided ymnastics to master the use of the bed-pan. A suitable commode at the bedside esults in a smaller expenditure of energy. The experienced nurse will modify ner methods as much as possible to avoid disturbing the patient: there are imes when sleep is more important than regular meals, and the ritual of earlynorning washing and bathing can sometimes be relaxed.

Sleep.—The correction of insomnia is of the utmost importance Morphine is not a true hypnotic, but by its central action it relieves respiratory distress and allows the patient to sleep Time and again patients will say after an adequate dose that it has provided them with the first night's rest for weeks or even months. In the early evening the patient should be given hypodermically a dose of 10 to 15 mg ($\frac{1}{6}$ to $\frac{1}{4}$ gr) of morphine sulphate, and this repeated if [illegible] four or six hours An energetic attempt should be made to ensure a [illegible] important that it [illegible]

[illegible]

the nurse having instructions to repeat [illegible]

The potency of chloral can, if necessary, be enhanced by the addition of 0 6 to 1 2 ml (10 to 20 min.) of the tincture of opium

On account of their reliability and ease of administration, the various barbiturate preparations have shown a tendency to replace the chloral of former days in the correction of cardiac insomnia. Phenobarbitone or its soluble sodium salt may be given at night in doses of 0 1 g ($1\frac{1}{2}$ gr.) in tablet form. Ampoules, each 1 ml of a 20 per cent solution containing 0 2 g. (3 gr.), are also available for *intramuscular* injection This makes a convenient substitute for the subcutaneous injection of morphia, which it may replace after the first few days

[illegible] these first few days the doctor will visit his patient preferably twice [illegible] one is the more [illegible] y to ensure sleep. It is worth aiming at a total [illegible] twenty-four as a *minimum, but the drug selected and its dose will be largely determined by the patient's general condition, the amount of sleep obtained during the day and the degree of breathlessness, these considerations are of greater importance than any physical sign revealed by examination of the heart.*

Dietetic Treatment

In arranging a diet for his patient the doctor will bear in mind the desirability of restricting the total calories in order to reduce metabolism and decrease the work of the heart. On account of portal congestion large meals are badly tolerated; indeed, anorexia, nausea and vomiting often present special problems

of their own. The restriction of protein to 50 or 60 g. daily, an amount sufficient to compensate for nitrogen loss, reduces its specific dynamic stimulus to metabolism to negligible proportions. Fats as a rule are poorly tolerated, particularly so when jaundice—a fairly frequent accompaniment of the most advanced form of congestive failure—complicates the picture. [illegible]
supply of energy
frequent feeds.
Restriction of fl [illegible]
sufficient to quench thirst. When salt intake is limited, 2 to 3 litres of water may be consumed daily without harm.

The diet should be low in salt content, particularly salts of sodium, as clinical experience has taught that the sodium ion is of more importance than the chloride in the retention of tissue fluid. [illegible]

become unpalatable, but the salt substitutes on the market are best avoided, as they may produce toxic symptoms. It is as a rule sufficient to advise that salty and spicy articles of food be omitted from the diet, that as little salt as possible be used in cooking, and that salt be not served with meals. Few patients begin to complain about lack of salt until the end of the first week or ten days of treatment, by which time their œdema is usually relieved.

For the severest grades of congestive failure, the Karell diet has much to recommend it, at least for the first few days of treatment. The procedure, in its strictest form, permits nothing by mouth except 800 ml. milk daily. Such a [illegible]

[illegible] and after twenty-four or forty-eight hours of the strict Karell diet [illegible]

If progress has been satisfactory, as shown by a fall in weight and an increased urinary output, a more generous diet can be substituted. An increased [illegible]

DIET No. 1

Approx. 1·25 g. Na. 1,700 Cals. NaCl 4 g.

Breakfast—
1 egg or small piece of white fish.
2 slices of bread.
Jelly marmalade if desired
Butter from allowance.
Tea with sugar, and milk from allowance.

Mid-morning—
Glass of fruit juice.

Dinner—

Small helping of lean meat, fish, tripe, chicken or rabbit.
Avoid ketchups and sauces.
Small helping of sieved vegetables.
Small helping of mashed potato.
Stewed fruit, fresh fruit jelly, fruit whip or snow with sugar *ad lib.*

Tea—

1 slice of salt-free bread.
Very small helping of meat or chicken or fish, or an egg.
Salt-free margarine.
Jelly if desired.

Supper—

1 slice of salt-free bread.
Jelly if desired.
Salt-free margarine.

Bedtime—

Glass of fruit juice.

Allowance for Day—

½ pint of milk
¾ oz of salt-free margarine or butter.

Provided the patient is not obese, as much sugar or glucose as desired may be added to the diet.

All food should be cooked without salt and no salt served with meals.

Meat, Fish—Avoid all tinned and preserved meat, including ham, bacon, sausages; kippers, finnan haddock; meat extracts as Oxo and Bovril, also Marmite, because of their high salt content.

Fruit—All fresh fruit is suitable, but dried fruit often contains too much salt.

To be successful the low sodium diet requires detailed care, and note should be taken of the following considerations:

Special Instructions:

(1) In the preparation of the food no salt is to be added during cooking or served with the meal at table.

(2) All tinned foods which have salt already added, such as tinned meats and vegetables, tinned soups and tomato juice, are to be avoided.

(3) Smoked, brine-cured and salty foods such as bacon, ham, sausages, smoked fish, kippers and pickles, are not permitted. This applies also to meat extracts and sauces such as Bovril, Oxo, Marmite, ketchup and relishes.

(4) Shellfish such as oysters and lobsters are not permitted

(5) Only breads prepared with yeast and made without salt are allowed. Cheese is not permitted.

(6) Foods to which baking-powder or baking-soda has been added in their preparation are not permitted. This includes biscuits, wafers, scones, "cookies" and cakes.

(7) Only unsalted or "washed" butter is allowed.

(8) Dried fruits such as figs, dates, raisins, apricots and prunes are to be avoided.

(9) It is particularly important that no sodium-containing medicines be taken while the diet is in use This includes sodium bromide, sodium bicarbonate, soda mints and most of the so-called " indigestion " tablets and powders Similarly, " soda-water " must not be added to drinks Salt gargles and toothpastes containing sodium are likewise forbidden.

Recipe for Salt-free Bread—If salt-free bread cannot readily be obtained, it can be made according to the following recipe :

6½ lb bread flour.
10 oz sugar.
8 oz. shortening.
4 oz yeast.
2 quarts of water.

This makes six loaves This bread takes a little longer to rise than ordinary bread.

Foods Permitted ·

(1) Meat, boiled fish or poultry, prepared and served without added salt.

(2) Eggs—not more than one daily

(3) Milk—limited to two glasses (one pint as a maximum)

(4) Vegetables—any fresh or green vegetables prepared and served without salt.

(5) Fruits—all fresh and tinned or stewed fruits.

(6) Bread—only yeast bread prepared without salt.

(7) Cereals—the only dry prepared cereals permitted are puffed wheat, shredded wheat and puffed rice

(8) Potatoes and rice prepared without salt

(9) Butter—only unsalted or " washed ".

(10) Puddings and sweets—custards, junket and plain puddings made with the milk allowance and with no added salt Pies with no salt added to the pastry and limited to a filling prepared with fresh or tinned fruit Jellies, jams, marmalade, white or brown sugar and honey.

(11) Drinks—tea, coffee, fruit juices and carbonated drinks.

(12) Flavourings—chocolate, cocoa, caramel, peppermint, lemon, orange, vanilla, cherries, cloves, cinnamon, nutmeg, ginger and coffee.

(13) Seasonings—pepper, curry, mustard, mint, vinegar, sage and onion.

[illegible]

kept below 1 g. in the twenty-four hours.

Patients vary in their tolerance to salt restriction. Many become habituated [illegible]

for more than two or at most three consecutive weeks. The dangers of uræmia, a consequence of salt depletion, are very real. The addition of salt to the diet for

a few days at a time has therefore the approval of clinical experience, and consoles the impatient who all too commonly exclaim with Job (vi. 6-7): "Can that which is unsavoury be eaten without salt? or is there any taste in the white of an egg? The things that my soul refused to touch are as my sorrowful meat."

recognizing that brisk purgation is exhausting and does little to relieve congestion. *Diarrhœa weakens the patient. A daily bowel movement is sufficient.*

The stool which results is of almost normal consistence, and is unassociated with pain or colic. Many of the proprietary salines in common use contain sodium chloride or other salts of sodium, and though more agreeable to take than magnesium sulphate, are best avoided. For similar reasons, should an enema be *required, 150 to 300 ml (5 to 10 fl. oz) of warm olive oil, to which one or two* teaspoonfuls of turpentine may be added, slowly injected and retained for some hours, is preferable to the discomfort associated with liberal quantities of soap and water.

It is important to note that, acting on the principles outlined above, remarkable improvement may become evident in the course of a few days Many

in assessing the *prognosis. Even a partial diuresis induced by rest and diet* without the use of digitalis betokens a favourable response to further treatment.

The Use of Digitalis

In the past, too much attention has been focused on the use of digitalis and too little on the other measures used in the treatment of congestive failure. Nevertheless, if full advantage is to be obtained from this remarkable drug, it is important to have a sound knowledge of the mode of its action, the indications for its use and how to regulate its dose. Digitalis should never be prescribed haphazardly.

Preparations in Common Use.—The dried leaves of the purple-flowered foxglove are the source of the three crude pharmacopœal preparations. The infusion on account of its bulk is now seldom prescribed: the tincture has largely given place to tablets, pills or capsules, each containing commonly 0 1 g. of powdered digitalis leaf. Accuracy of dosage and convenience of administration are achieved by prescribing the drug as tablets of the compressed powdered leaf. Dispensed in this way the dose is readily adjusted according to individual requirements.

The leaf of *Digitalis purpurea* yields the glycosides digitoxin, gitalin and gitoxin, whereas the yellow-flowered foxglove, *Digitalis lanata*, contains in its leaf three glycosides, lanatoside A, B and C, from which on hydrolysis are [illegible] d from both [illegible] *ata*, are two [illegible]

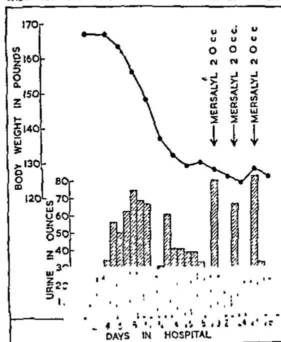


FIG 2

[illegible]

From the seeds of *Strophanthus kombé*, from which the African arrow-poison was produced, the glycoside strophanthin K is obtained Similarly the related [illegible]

for the drug In recent years the use of the isolated active principles has increased and it is therefore necessary to be familiar with digoxin, digitoxin and ouabain—the glycosides commonly substituted in this country for the whole leaf. All

these preparations are similar in their fundamental effects on the heart and circulation, but they differ in their speed of action, degree of absorption from the gastro-intestinal tract, in the duration of their effect and the rate of their destruction. (See table, p. 537.) Digoxin and ouabain have the advantage *that they are suitable for intravenous injection by which in an emergency* a prompt effect on the heart can be obtained in the course of a few minutes. By contrast, 24 to 48 hours elapse before a full effect is obtained from maximum oral doses of the whole leaf.

[illegible]
acti [illegible]
mus [illegible]
ful contraction and an increased output per beat. These effects outweigh the benefits attributable to slowing of the heart rate. In heart failure with normal sinus rhythm improvement commonly occurs without significant slowing of the heart, or becomes evident before any change in heart rate takes place. By more effective pumping the accumulated venous return is accepted, the cardiac output correspondingly increased and compensation restored.

In heart failure with auricular fibrillation tachycardia is common, the ventricular rate ranging between 80 and 160 or more per minute. Slowing of the heart rate is usually a conspicuous feature of digitalis action when auricular fibrillation is accompanied by a fast ventricular rate. By impairing auriculo- [illegible]

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[illegible] indicates that it is in low-output [illegible] it. The rheumatic, hypertensive and arteriosclerotic varieties of *congestive heart failure* are those in which its greatest usefulness is found. Less satisfactory results are obtained in the high-output failures associated with chronic pulmonary disease, hyperthyroidism and anæmia. Under certain circumstances digitalis may appear to aggravate failure when the cause is other than intrinsic heart disease. In the presence of active infection, for example, the acute carditis of rheumatic fever, diphtheria or pneumonia, digitalis is usually ineffective and may prove harmful. If digitalis is employed in these forms of heart failure, it must be used with caution in small doses and repeated observations made for signs of toxicity. When auricular fibrillation is present, particularly with high ventricular rates, a satisfactory response to digitalis can be anticipated as a rule—particularly if rheumatism is the cause of the underlying heart disease—but a slow regular pulse, even that of complete heart-block, is not a contra-indication to its use if signs of congestive failure are present.

Great benefit can be obtained from its use in the treatment of *left ventricular failure* both in an acute and chronic form. Thus acute attacks of paroxysmal nocturnal dyspnœa ("cardiac asthma") can often be promptly relieved by its use, and the more chronic manifestations of left-sided failure (exemplified by exertional dyspnœa with minor degr[illegible] congestion restricted to the bases of the lungs) are also responsive as a re[illegible] power to restore ventricular output. Its long-term u[illegible] these circu[illegible] [illegible] the day-to-day tendency to

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The use of the drug except in these circumstances finds little or no support in clinical experience A rapid heart beat is not in itself an indication for digitalis. The drug is contra-indicated in the acute peripheral circulatory failure of shock and collapse in which it neither elevates the blood pressure, increases the cardiac output nor slows the heart There is no justification for its use before or after surgical procedures unless congestive failure appears imminent or is already present.

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Digitalis Action.—All the galenical preparations of digitalis, and the three active principles, digoxin, digitoxin and ouabain, act directly on the heart muscle. Thus stimulated, the ventricular myocardium produces a more powerful contraction and an increased output per beat. These effects outweigh the benefits attributable to slowing of the heart rate. In heart failure with normal sinus rhythm improvement commonly occurs without significant slowing of the heart, or becomes evident before any change in heart rate takes place. By more effective pumping the accumulated venous return is accepted, the cardiac output correspondingly increased and compensation restored.

In heart failure with auricular fibrillation tachycardia is common, the ventricular rate ranging between 80 and 160 or more per minute. Slowing of the heart rate is usually a conspicuous feature of digitalis action when auricular fibrillation is accompanied by a fast ventricular rate. By impairing auriculo-ventricular conduction and by increasing the refractory period of the myocardium, the output is improved and the ventricular rate progressively diminished. The pulse-deficit is thereby abolished and peripheral blood flow increased. With the improvement in the mechanical efficiency of the heart, the cardiac output rises, renal blood flow improves, diuresis is induced, œdema fluid is mobilized, [illegible] -weight falls.

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Digitalization.—It has been estimated that on the average the body destroys or excretes digitalis at a fairly steady rate, ranging around 0 1 g (1½ gr.) or less of the powdered leaf per day When the daily dose exceeds this quantity a proportion accumulates in the tissues so that the concentration rises step by step until the saturation point is reached. In general, the greater the body-weight the more digitalis is required for this purpose. Over-saturation is indicated by the production of symptoms and signs of digitalis intoxication. Maximum benefit is obtained by a concentration just short of the toxic amount. The patient is then said to be fully digitalized.

If a small single dose of less than 0 1 g of the powdered leaf is taken daily by a man of average weight, say 72 kg (160 lb), an effective concentration in the tissues may never be obtained, for just as much is eliminated or destroyed each day as is given to the patient. Individuals vary greatly in their tolerance and in their requirements, but as a general rule seven to ten consecutive days will elapse before a daily dose of 0 4 g. (6 gr) reaches a concentration sufficient to induce maximum benefit. This quantity is just short of that which induces the usual toxic symptoms—headache, anorexia, nausea and vomiting. By doubling the

daily dose, say to [illegible]

lag is reduced further and the first symptoms of digitalis poisoning may be observed in twenty-four to forty-eight hours. It is thus apparent that an effective therapeutic concentration of the drug depends on the rate with which successive doses are administered. On account of its slow destruction and excretion, at least fourteen days will elapse before the tissues are fully desaturated. It is for this reason that large doses must be avoided in those patients who have been taking digitalis within the previous two weeks In the treatment of heart failure allowance is made for the property of the drug to accumulate.

Methods Employed.—By [illegible] methods employed to digitalize [illegible] severity of his condition. (*a*) [illegible] distress, and the doctor knows that no digitalis or related preparations have been taken in the preceding ten or fourteen days, then an unusually large quantity may be administered by mouth, even 1 to 1 5 g. (15 to 25 gr.) of the powdered leaf as a single dose to a man of 72 kg. (160 lb.) or more. A suitable massive [illegible] 100 mg. (1 to 1½ gr.) of [illegible], the full quantity being [illegible] lb will tolerate 1·5 g, preferably divided into two or three doses, within a twenty-four hour period. A corresponding dose of the tincture of digitalis, calculated on the basis of 1 ml. for each 4·5 kg (10 lb) of body-weight is 15 ml. Rapid digitalization by this method has many advantages and may be supplemented after forty-eight hours by further small oral doses, 0 1 g. twice or thrice daily.

(*b*) When the patient's symptoms are mild and his distress minimal, rapid and intensive digitalization is neither justified nor required Small, regular [illegible]

appear—usually within a week or ten days from the start of treatment.

(*c*) Between these two extremes fall the majority of patients admitted to hospital in congestive heart failure. They are moderately distressed and it is often not known whether digitalis has been employed in their treatment within the preceding ten or fourteen days. In these circumstances it is often justifiable to withhold digitalis for a few days so as to judge of the effect of rest in bed, nursing care, better sleep and a suitable diet (see Fig 2). If substantial improvement is not obvious within three or four days, then digitalization is indicated.

A procedure which combines the advantages of fairly rapid digitalization with subsequent adjustment of the dose to the individual's particular requirements is to commence treatment with a single comparatively large dose of say 0 5 to 0 8 g. of the powdered leaf and six to eight hours afterwards continue with small doses as already recommended for the patient less acutely ill—perhaps 0·1 g. thrice daily These small doses are repeated regularly until the earliest toxic manifestations appear. At this point the drug is at once discontinued In this way the patient is brought under the influence of the drug quickly, and by continuing with smaller doses full effects are obtained in three or four days. The method may be compared to a simple titration in the laboratory. When the strength of the solution to be tested is roughly known, it is permissible to run

abruptly from the burette a large quantity of the reagent, and thereafter continue cautiously drop by drop until the end-point is determined with accuracy.

The Response to Digitalization.—As the concentration of the glycosides rises in the myocardium, and for some few days thereafter, remarkable improvement is usually observed. The signs of congestive failure subside: the venous pressure decreases, dyspnœa lessens, comfort is found in longer and sounder sleep, diuresis begins and, with the dispersal of the excess tissue fluid, the body-weight falls. As a guide to the efficacy of digitalis therapy, records of body-weight and urine output are most helpful. When the patient is beginning to improve, he loses weight (see Figs. 2 and 3). Conversely, a sudden gain in weight is commonly the first indication of further retention of fluid. In hospital most patients with congestive heart failure should be weighed on alternate days. It does them good to be helped out of bed even for a minute or two every few days. When the patient has recovered sufficiently to return home, he should weigh himself weekly. He has then a measure of his progress, and his diet and drug therapy can be adjusted accordingly.

There are other signs of improvement which are worth noting. The diuresis of digitalization is usually maintained for several days. For this reason urinary outputs should be recorded every twenty-four hours. For bedridden patients who cannot be weighed accurately, the specific gravity of the urine can also be used as a measure of progress. It is high in the presence of failure and falls with the onset of diuresis. The size of the liver can be determined in a rough and ready way by clinical means. As the circulation improves, its size decreases. Similarly, the subsidence of pulmonary œdema in left-sided heart failure is accompanied by higher readings of vital capacity. The ventricular rate should be counted and charted daily. Remarkable slowing may be observed when auricular fibrillation accompanies congestive failure. As much relief may be obtained from digitalization in similar grades of failure with normal rhythm in which slowing of the heart may not amount to more than 10 or 20 beats per minute. As a measure of the patient's response to treatment, however, brady-cardia is less impressive than the increased bodily comfort and restored sense of well-being—subjective effects which are none the less real though they defy accurate analysis and precise measurement. There are better guides to the response to digitalis than the rate of the heart.

Digitalis Intoxication.—Until the patient is familiar with the effects of digitalis, by which he may ultimately learn to regulate his own dosage very effectively, the doctor should have him under observation from day to day. Every preparation of digitalis, and all the related cardiac glycosides which exert a therapeutic effect, will produce toxic effects if given in adequate doses for a sufficiently long time. In fact, therapeutic digitalization is the maximum quantity tolerated short of signs of intoxication. Hence the importance of their early recognition.

The first symptoms to appear are almost invariably headache and loss of appetite. Six or eight hours later, if the administration of digitalis is continued, nausea and vomiting occur which are peculiarly distressing to the patient on account of the associated retching. The drug should be stopped at the earliest indication of saturation and thereby the exhaustion, fatigue and mental depression which accompany continued vomiting will be avoided. Yellow and green vision occasionally occur. More commonly in elderly patients, disorientation, delirium and visual hallucinations, often taking the form of rectangular figures, cause

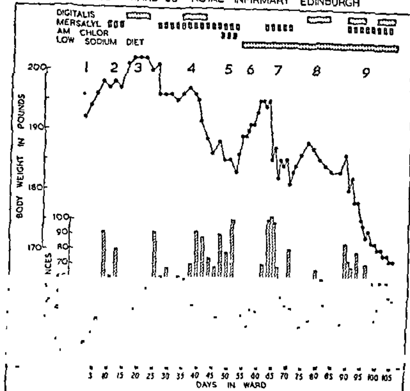


Fig 3

To show how in advanced congestive heart failure a satisfactory response to treatment may be obtained under the influence of a number of remedies when the effect of each separately is incomplete or unsatisfactory

The patient was a man aged 51, suffering from a severe grade of congestive heart failure associated with complete heart-block of arteriosclerotic origin His weight and urine outputs were charted from the day of admission to hospital until he was œdema-free 105 days later. He was confined to bed throughout the entire period of observation A rough estimate of the value of the various measures employed, either singly or in combination, can be made *according to the following scheme :*

Period	*Treatment Employed*	*Weight Loss or Gain*	
1	Rest+light diet, Na 1 6 g	—	Gain 6 lb
2	Rest+light diet+mersalyl	—	—
3	Rest+light diet+digitalis	—	*Gain 5 lb*
4	[illegible]	*Loss 15 lb.*	—
5	[illegible]	*Loss 3 lb.*	—
6	[illegible]	—	*Gain 12 lb.*
7	[illegible]	*Loss 14 lb*	—
8	[illegible]	*Loss 6 lb.*	—
9	[illegible]	*Loss 18 lb*	—

... bed rest and a salt-restricted diet (Na 1 6 g daily) failed to disperse the ... With the addition of mersalyl injections ...

concern. Gastro-intestinal and central symptoms of the type just described usually precede local cardiac signs of digitalis poisoning, but there are exceptions to this rule.

The most common [illegible] referable to the heart is the production of [illegible] [illegible] heart beat. If digitalis administration is continued in these circumstances more serious disturbances are liable do develop, in particular ventricular paroxysmal tachycardia which in turn may lead to ventricular fibrillation

Paroxysmal ventricular tachycardia is liable to occur in arteriosclerotic patients, commonly the subjects of advanced myocardial fibrosis, handicapped by the more advanced grades of congestive heart failure, in whom the response to the drug has been unsatisfactory, with the result that its administration has been prolonged and excessive The influence of digitalis in the production of this serious and commonly fatal arrhythmia is shown in Fig. 4. Attacks may at

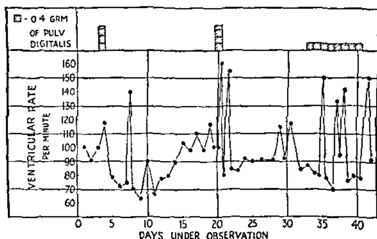


FIG 4

To show the relation of attacks of paroxysmal ventricular tachycardia to large and small doses of digitalis in an elderly man, the subject of an extreme degree of congestive heart failure refractory to all therapeutic measures Electrocardiograms confirmed the diagnosis Seven paroxysms were recorded

(From *Edin med J*, 1939, XLVI, p 249)

first be symptomless, but should be suspected by the presence of a heart rate usually in excess of 150 per minute A marked pulse deficit and an absence of any complaint of palpitation explain why shorter attacks may readily pass undetected The persistence of paroxysmal ventricular tachycardia for more than a few hours usually leads to an advance in the degree of congestive failure, and the production of cerebral symptoms, ranging from confusion to epileptiform attacks. Death is common.

The irregularity associated with partial heart-block, when of sufficient degree to cause an occasional " missed-beat ", can be suspected by feeling the pulse and

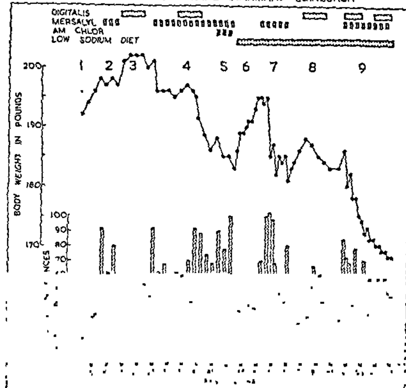


Fig 3

To show how in advanced congestive heart failure a satisfactory response to treatment may be obtained under the influence of a number of remedies when the effect of each separately is incomplete or unsatisfactory

the value of the various measures employed, either singly or in combination, can be made according to the following scheme.

Period	*Treatment Employed*	*Weight Loss or Gain*	
1	Rest + light diet, Na 1 6 g.	—	Gain 6 lb.
2	Rest + light diet + mersalyl	—	—
3	Rest + light diet + digitalis	—	Gain 5 lb
4	Rest + light diet + mersalyl + digitalis	Loss 15 lb.	—
5	Rest + light diet + mersalyl + dig + amm. chlor.	Loss 3 lb.	—
6	*Rest + low sodium diet, Na 0 89 g.*	—	*Gain 12 lb.*
7	Rest + low sodium + mersalyl	Loss 14 lb.	—
8	Rest + low sodium + digitalis	Loss 6 lb.	—
9	Rest + low sodium + mersalyl + digitalis	Loss 18 lb.	—

In this patient bed rest and a salt-restricted diet (*Na 1 6 g* daily) failed to disperse the

concern. Gastro-intestinal and central symptoms of the type just described usually precede local cardiac signs of digitalis poisoning, but there are exceptions to this rule.

Th[illegible] heart beat. If digitalis administration is continued in these circumstances more serious disturbances are liable to develop, in particular ventricular paroxysmal tachycardia which in turn may lead to ventricular fibrillation.

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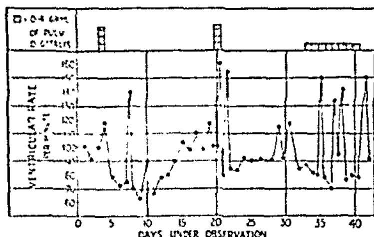


FIG. 4

To show the relation of attacks of paroxysmal ventricular tachycardia to large and small doses of digitalis in an elderly man, the subject of an extreme degree of congestive heart failure refractory to all therapeutic measures. Electrocardiograms confirmed the diagnosis. Seven paroxysms were recorded.

(From *Edin. med. J.*, 1939, XLVI, p. 249)

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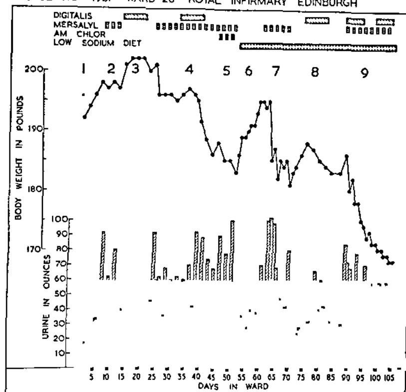


FIG 3

To show how in advanced congestive heart failure a satisfactory response to treatment may be obtained under the influence of a number of remedies when the effect of each separately is incomplete or unsatisfactory

The patient was a man aged 51, suffering from a severe grade of congestive heart failure associated with complete heart-block of arteriosclerotic origin His weight and urine outputs were charted from the day of admission to hospital until he was œdema-free 105 days later He was confined to bed throughout the entire period of observation A rough estimate of the value of the various measures employed, either singly or in combination, can be made according to the following scheme .

Period	*Treatment Employed*	*Weight Loss or Gain*	
1	Rest + light diet, Na 1 6 g.	—	Gain 6 lb
2	Rest + light diet + mersalyl	—	—
3		—	Gain 5 lb.
4		Loss 15 lb.	—
5		Loss 3 lb	—
6		—	Gain 12 lb
7	Rest + low sodium + mersalyl	Loss 14 lb	—
8	Rest + low sodium + digitalis	Loss 6 lb.	—
9	Rest + low sodium + mersalyl + digitalis	Loss 18 lb.	—

In this patient bed rest and a salt-restricted diet (Na 1 6 g daily) failed to disperse the

concern. Gastro-intestinal and central symptoms of the type just described usually precede local cardiac signs of digitalis poisoning, but there are exceptions [illegible]

[illegible]

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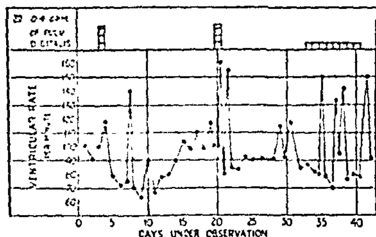


Fig. 4

To show the relation of attacks of paroxysmal ventricular tachycardia to large and small doses of digitalis in an elderly man [illegible] degree of congestive heart failure refractory to all therapeutic meas[illegible] Seven [illegible]

(From *Edin. med. J.*, 1939, [illegible])

first be symptomless, but should be suspected by the presence of a heart rate usually in excess of 150 per minute. A marked pulse deficit and an absence of any complaint of palpitation explain why shorter attacks may readily pass undetected. The persistence of paroxysmal ventricular tachycardia for more than a few hours usually leads to an advance in the degree of congestive failure, and the production of cerebral symptoms, ranging from confusion to epileptiform attacks. Death is common.

The irregularity associated with partial heart-block, when of sufficient degree to cause an occasional " missed-beat ", can be suspected by feeling the pulse and

recognized with greater certainty by auscultation of the heart. From the nature ... te heart- ... beating ... ntricular

tachycardia and extrasystoles may respond to the oral administration of potassium chloride in a dose of 5 to 10 g., or 1 g can be given intravenously as 10 ml. of a 10 per cent solution at a rate of 1 ml. per minute. For the relief of persistent *vomiting, cocaine in a dose of 30 mg. with bismuth* carbonate 1 to 2 g., can be taken by mouth three or four times a day. It is seldom required.

The Digitalis Glycosides.—These drugs are powerful and prompt in action, but have their individual peculiarities. All exert a digitalis-like action. Digoxin, a breakdown product of lanatoside C, is chemically pure, and when given intravenously produces an effect on the heart rate which is maximal within one to two hours. It is the remedy of choice for intravenous use in an emergency. Ouabain is even faster in action when given by this route. It is such a powerful drug that a total quantity of 1 mg. should not be exceeded in the twenty-four hours, and 1 mg. should never be administered as a single dose *if any digitalis has been taken by the patient within the previous two weeks.* On account of the risk of serious toxic symptoms, it is usually recommended that after an initial intravenous dose of 0·5 mg. of ouabain, further doses of 0·1 mg. at half-hourly or hourly intervals should be given until the desired effect is obtained. In this way the risk of overdosage by the intravenous route can be avoided. Strophanthus preparations are absorbed so irregularly and erratically from the gastro-intestinal tract that their oral use is not advisable.

The glycosides ouabain and digoxin are effective agents in an emergency. Twenty-four hours after the intravenous injection of 1 mg. of ouabain and six to twelve hours after 1 mg of digoxin, 0 1 to 0 2 g. of digitalis powder or 0 25 *mg. of digoxin in tablet form may be commenced three times a day by mouth.* Intravenous digoxin is particularly convenient for rapidly preparing the patient for further digitalization. It is soluble in alcohol, in which it is dispensed in ampoules. Immediately before use the alcoholic solution is diluted with ten times its volume of sterile water.

The accompanying table (see p 537) provides a ready contrast of the

resemble the parent substance, are in sharp contrast to digoxin and ouabain.

Ineffective Preparations.—There are other preparations of digitalis and digitalis-bodies on the market. Some are of undoubted value. Some are virtually inactive. It is well that the doctor should familiarize himself with a few reliable and potent preparations, such as those described on page 537, in which he can have trust There are no intravenous preparations superior to

Preparation	*Digitalis*	*Digoxin*	*Digitoxin*	*Ouabain*
Source	*Digitalis purpurea*	*Digitalis lanata*	*Digitalis purpurea*	*Strophanthus gratus*
Purity	variable, saponins, fats, etc.	chemically pure	relatively pure—95%	chemically pure
Absorption by oral route	poor	fairly complete	almost complete	erratic
Maximum single dose				
(1) Oral	1.5 g	1.5 mg	1.2 mg	unsuitable
(2) Intravenous	unsuitable	1 mg	1.2 mg	1 mg
Speed of action (Maximum effect)				
(1) Oral	24-48 hours	6-8 hours	10-12 hours	unsuitable
(2) Intravenous	unsuitable	1-2 hours	*6-10 hours*	½-2 hours
Duration of action	prolonged 2-3 weeks	short 3-5 days	prolonged 2-3 weeks	short 2-3 days
Maintenance daily oral dose	0.1-0.2 g	0.5-0.75 mg	0.1-0.2 mg	unsuitable
Dispensed:				
(1) Oral use	*powder in pills or tablets*	tablets 0.25 mg.	tablets 0.1 and 0.2 mg.	unsuitable
(2) Intravenous use	unsuitable	ampoules 0.5 mg in 1 ml. alcohol	unnecessary	(a) 0.5 mg. in 2 ml. ampoules (b) 0.1 mg. in 0.5 ml. ampoules

Table 1 contrasts the properties of digitalis leaf with the glycosides digoxin, digitoxin and ouabain. On account of their rapidity of action, digoxin or ouabain are preferable for intravenous use.

recognized with greater certainty by auscultation of the heart. From the nature of things, it can only occur in the presence of normal rhythm. Complete heart-block, on the other hand, may occur either in patients with regularly beating auricles or with auricular fibrillation. In the latter instance the ventricular

chloride in a dose of 5 to 10 g., or 1 g. can be given intravenously as 10 ml. of a 10 per cent. solution at a rate of 1 ml. per minute. For the relief of persistent vomiting, cocaine in a dose of 30 mg. with bismuth carbonate 1 to 2 g., can be taken by mouth three or four times a day. It is seldom required.

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The accompanying table (see p. 537) provides a ready contrast of the properties of the powdered leaf, and *the glycosides digoxin, digitoxin and ouabain.* Digitoxin, which is sold under various tr
and Digitaline (Nativelle), is a reliable
intravenous use. Its prolonged action

virtually inactive.
few reliable and
which he can have

Preparation	*Digitalis*	*Digoxin*	*Digitoxin*	*Ouabain*
Source	*Digitalis purpurea*	*Digitalis lanata*	*Digitalis purpurea*	*Strophanthus gratus*
Purity	variable, saponins, fats, etc.	chemically pure	relatively pure—95%	chemically pure
Absorption by oral route	poor	fairly complete	almost complete	erratic
Maximum single dose				
(1) Oral	1·5 g	1·5 mg	1·2 mg	unsuitable
(2) Intravenous	unsuitable	1 mg	1·2 mg	1 mg
Speed of action (Maximum effect)				
(1) Oral	24-48 hours	6-8 hours	10-12 hours	unsuitable
(2) Intravenous	unsuitable	1-2 hours	6-10 hours	½-2 hours
Duration of action	prolonged 2-3 weeks	short 3-5 days	prolonged 2-3 weeks	short 2-3 days
Maintenance daily oral dose	0·1-0·2 g	0·5-0·75 mg.	0·1-0·2 mg	unsuitable
Dispensed				
(1) Oral use	powder in pills or tablets	tablets 0·25 mg.	tablets 0·1 and 0·2 mg.	unsuitable
(2) Intravenous use	unsuitable	ampoules 0·5 mg. in 1 ml. alcohol	unnecessary	(a) 0·5 mg in 2 ml ampoules (b) 0·1 mg in 0·5 ml. ampoules

Table 1 contrasts the properties of digitalis leaf with the glycosides digoxin, digitoxin and ouabain. On account of their rapidity of action, digoxin or ouabain are preferable for intravenous use.

digoxin or ouabain, and the pharmacopœal powder is as reliable as any oral preparation on the market.

It is important that the doctor should distinguish clearly between digitalin [illegible]

Digitalin in the usual oral or subcutaneous dose of 0·6 mg ($\frac{1}{100}$ gr.) as dispensed by the manufacturers is entirely valueless. In point of fact, its effective oral dose is 30 to 60 mg. ($\frac{1}{2}$ to 1 gr.) and its effective parenteral dose 5 to 10 mg. ($\frac{1}{12}$ to $\frac{1}{6}$ gr.)—*quantities which are seldom if ever prescribed in this country.* It is unfortunate and confusing that tablets of digitalin 0·6 mg. $\frac{1}{100}$ gr.) continue to be included amongst selections of drugs offered by the manufacturing chemists for emergency use. With other potent and highly effective glycosides available—digoxin, digitoxin and ouabain—it is unjustifiable to order digitalin, and least of all in a dose 100 times less than the effective oral quantity, or 20 times less than the effective parenteral dose.

Maintenance Dosage.—When the optimum response has been achieved by the initial course of digitalis treatment, it is almost always important to maintain a continued state of therapeutic saturation by administering small daily doses of the drug in a quantity a little greater than the amount excreted or destroyed by the body. *In this way the improvement already achieved may be* maintained and further progress recorded. Just as the initial digitalizing dose is adapted to the patient's individual requirements, so also maintenance dosage must be adjusted according to his needs and his tolerance.

When full digitalization from the initial doses is first achieved, the drug should be stopped for at least four days. Thereafter 100 mg. ($1\frac{1}{2}$ gr.) of the powdered leaf, preferably in pill or tablet form should be given thrice daily. This quantity is continued until the first toxic symptoms—headache or anorexia—reappear. Again, the drug is stopped and the patient asked to note the number of days elapsing between the start of maintenance doses and their discontinuation. [illegible] a second course will be of approximately the same [illegible] *a few doses* [illegible] e course is [illegible] which the [illegible] ie quantity of the medicament consumed each day. In many ways a short course of five consecutive days, followed by a pause of two days on which no digitalis is taken, has advantages as it lends itself to such an easily remembered routine, all medication being omitted on two days, say Saturday and Sunday each week. By increasing, or more commonly, decreasing, the daily quantity of digitalis recommended above for the first maintenance course, it is usually possible to adapt the dose to a simple routine which will provide the maximum benefit and the minimum inconvenience for the *particular individual.*

[illegible] dosage. By [illegible]

to suppose that, on account of nausea or vomiting, he is [illegible]

The doctor's duty is to explain to the patient how to discover the optimum quantity of the drug he can tolerate

Reasons for withholding Digitalis.—It is worth repeating that digitalis [illegible]

œdema, the acute congestive failure of paroxysmal auricular fibrillation, or in chronic congestive failure when the patient is desperately ill, is particularly dangerous if even partial digitalization has been achieved in the preceding days. Great care is then required, and if the intravenous route is used, then the usual dosage should be halved If in doubt it is wiser to withhold digitalis for some days.

[illegible] mia, or hyper- [illegible] iably, unsatis- [illegible] digitalis may reduce the venous pressure, but any improvement in cardiac output is exceptional and indeed the output may fall further to the patient's disadvantage. It is only in the most advanced stages of failure that a rise in cardiac output can be detected, and the treatment of this form of high-output failure is often best conducted by excluding digitalis from the therapeutic régime. In treatment emphasis deserves to be placed on the precipitating factors, and amongst these an acute exacerbation of chronic bronchitis is a frequent cause of congestive failure Hence the importance of using penicillin freely, even in the absence of fever, with the object of eradicating the acute infection and of administering oxygen generously to help overcome the inadequate pulmonary ventilation. Both these measures, supplemented by intramuscular mercurials and bronchial relaxants, are of the greatest importance in the treatment of cor pulmonale. Digitalis should be used with caution in view of the danger of aggravating [illegible]

thrombi from the ventricular cavities and of enhancing the clotting tendency of the blood. There are, therefore, those who countermand the use of the drug before the myocardial infarct has healed Nevertheless, if signs of congestive failure develop and are productive of symptoms, for example, sufficient breathlessness to cause discomfort, digitalis can be prescribed by the small dose method and discontinued as soon as relief is obtained, or earlier if toxic signs appear. *Its use is fully justified in these circumstances if employed with caution*

Finally, digitalis is sometimes withheld in the treatment of congestive failure in childhood, presumably on account of the unsatisfactory response recorded in failure attributable to the severest forms of acute rheumatic or diphtheritic carditis in children In these circumstances serious arrhythmias, including high-grade heart-block, sometimes fatal, may be provoked by even small doses of digitalis. Apart from this form of congestive failure, digitalis is not contra-indicated in childhood. The dose can be calculated on a body-weight basis

according to the method outlined on p. 532. For instance, a child of 14 kg. (30 lb.) can be digitalized with 0 3 g. (4½ gr.) of the leaf or 3 ml. of the tincture. The usual daily maintenance dose for a child is about one-tenth of the oral digitalizing dose.

Summary.—Having a clear indication for the use of digitalis, the doctor must ensure that his patient receives initially an amount appropriate to the urgency of the symptoms. The successful use of the drug involves repeated and accurate clinical observations in regard to its beneficial effects and its peculiar *toxic symptoms. To maintain* progress after full digitalization has been achieved, maintenance doses are usually necessary. Taken in a succession of short courses of a week or less with a few days intervening between each, digitalis can exert a beneficial effect for months or years without the production of toxic symptoms.

The Use of Diuretics

Diuretics are indicated in the treatment of congestive failure when, after a fair trial, the response to digitalis is incomplete or unsatisfactory. They are *therefore only essential in a minority of cases—the* number being inversely proportional to the physician's skill in the use of digitalis. As they are so efficient in action, mercurial diuretics are nowadays employed with increasing frequency even before the stage of full digitalization has been reached They enhance its action, but their diuretic effect is greater when the patient is fully digitalized.

Mercurial Diuretics.—*Indications*—Right-sided failure usually responds so well to organic mercurials that some alleviation of portal and peripheral congestion is promptly experienced The liver shrinks in size and the body-weight falls as the diuresis continues. The action of the drug begins in the course of an hour or two, reaches a maximum in eight to twelve hours and subsides in twenty-four to thirty-six hours. Urinary outputs of between 1,800 and 4,000 ml in the twenty-four hours following the injection are not uncommon.

In the treatment of the pulmonary congestion of left-sided failure mercurials are usually effective. Furthermore, both minor and major manifestations of acute left ventricular failure can often be prevented by a well-timed injection of the drug. The former are revealed by bouts of orthopnœa or intractable nocturnal cough and restlessness, and the latter by frank attacks of so-called " cardiac asthma " with or without acute pulmonary œdema. A record of body-weight is a helpful guide, particularly in the ambulant patient who has been rendered œdema-free. A sudden gain of 2 or 3 lb. often heralds a further nocturnal attack of cardiac asthma which can usually be averted by a timely injection of the mercurial compound. In the emergency of the acute attack of cardiac asthma mersalyl can be combined in the one syringe with digoxin and both administered together intravenously.

Mercurials are not a substitute for digitalis. They can unload a circulation overburdened by a swollen blood volume but they do not influence cardiac output. However, in the decompensated heart in cor pulmonale and in active carditis with congestive failure, to which reference has already been made, [illegible] effective treatment when there

[illegible] is *not*

increased, but the tubular reabsorption of water and electrolytes from the

filtrate is temporarily reduced with resultant increase in urinary flow. Sodium, potassium, calcium and chlorides are excreted in increased amounts. The mercurial diuretics have a pronounced effect on sodium excretion, the quantity

depletion of the body stores of salt after repeated use of the mercurial diuretics is particularly liable to occur, with serious consequences to the patient (see p. 105).

in order to compensate for the fall in blood volume. The net result is absorption of transudates, diminution of tissue œdema, with loss of water and electrolytes and a corresponding fall in body-weight.

Methods of Administration.—The injection of mersalyl (B.P.) is the preparation in common use in this country. It is dispensed in a 10 per cent. solution in 1 or 2 ml. ampoules containing a 5 per cent solution of theophylline in which it is freely soluble and which potentiates its diuretic action. The usual routine in the presence of congestive failure is to inject 1 or 2 ml either intravenously or intramuscularly on alternate days and preferably early in the forenoon. A better effect is obtained when the injection is made into an œdema-free area The solution should be deposited as deeply as possible. None should escape

drugs. Vigorous massage with a ball of cotton-wool over the site of the injection disperses the medicament and diminishes the local irritation. If this simple measure is insufficient to prevent pain and discomfort, 0·1 to 0·2 ml. (1½ to 3 min.) of 2 per cent. sterile procaine solution may be added to the syringe and needle already loaded with the mercurial preparation. The efficacy of the diuretic is not impaired by the addition of the local anæsthetic, which even in a dilute form is a very effective means of preventing the local pain of which thin and elderly patients often complain In more resistant cases of congestive failure and in the emergency of acute left ventricular failure, recourse must be made to the intravenous use.

Successive doses on alternate days should not be increased above 2 ml. They are usually continued until the patient's weight is steady and the tissues œdema-free. If maintenance doses of digitalis are in themselves insufficient during the convalescent period to control the tendency to congestive failure, mersalyl may be employed at weekly or bi-weekly intervals for months at a time. The ambulant patient will find a weight record at intervals of twice a week a good guide to his reponse to treatment.

Other preparations are available for oral, rectal and subcutaneous use. Novurit is a compound similar to mersalyl which is dispensed in suppositories containing 0·5 g. In suitable patients the rectal administration of mercury

in this form yields an excellent diuresis. It is an easy, effective and painless method of administering the drug, but internal hæmorrhoids or fissures may preclude its use on account of acute discomfort experienced an hour or two after the suppository has been *inserted. Tablets of mersalyl, each containing* 80 mg., may be taken three or four times a day with the object of supplementing the beneficial effects of intramuscular therapy. Their absorption often tends to be

which can sometimes be overcome by the use of ammonium chloride on alternate days

Contra-indications.—Renal insufficiency is the main contra-indication to the use of mercurial diuretics, in particular acute diffuse glomerulo-nephritis. In this condition mercury may cause an exacerbation of the kidney damage and lead to more serious difficulties, if not a fatal outcome. The presence of albuminuria with casts and red cells demands caution, though they may equally well result from passive renal congestion as from an acute nephritis The clinical history and the course of the illness will help to distinguish the presence of active renal disease.

Similarly, the renal insufficiency of congestive heart failure, if accompanied by a blood urea nitrogen in excess of 60 mg. per cent., is usually a contra-indication to giving mercury. In the presence of poor oral hygiene there should be some hesitation in using these drugs on account of the risk of serious stomatitis Colitis—an uncommon accompaniment of heart failure—is a contra-indication to mersalyl therapy.

In elderly men, the subjects of enlarged prostates, urinary retention or even uræmia may follow the initial profuse diuresis. Prostatism can be avoided to some extent by commencing with a small dose of the diuretic, say 0·5 ml. and increasing the quantity gradually

Toxic Effects.—The intensive use of these drugs may result in toxic effects directly attributable to poisoning with the heavy metal—mercurialism—or to hypersensitivity on the part of the individual patient. The salt depletion syndrome, discussed on p. 105, which is *the result of a profound disturbance of* the balance of the blood electrolytes arising in consequence of intensive and repeated diuresis, is to be distinguished from the toxic effects of mercury *per se.*

Mercurialism is the result of accumulation of mercury in the tissues. When the response to mersalyl is poor, the tendency is to increase the dose and frequency of the injections—a procedure which may lead to the retention of mercury in the body. If the diuresis induced exceeds 2 litres, 75 per cent. of the mercury injected is excreted in the urine within twenty-four hours. Daily

even as often as once or twice weekly for years at a time, apparently does no harm to the tubular epithelium

Hypersensitivity is occasionally acquired. Reactions such as chills, bursts of fever with or without actual rigors, are occasionally encountered. Skin eruptions are sometimes found to be attributable to these drugs. Dyspnœa, anxiety, *palpitation,* pallor and faintness experienced an hour or two after an intra-muscular injection should not be ignored. A change should be made in the

preparation used and the method of administration altered before the drug is abandoned.

Carbonic Anhydrase Inhibitors.—Within the last two years the carbonic anhydrase inhibitors, such as acetazoleamide (Diamox) have been employed. They cause an increased bicarbonate output, but the initial diuretic response declines as the bicarbonate in the blood becomes depleted. Theoretically these [illegible] nonale in [illegible] nd on the [illegible] daily on alternate days.

Xanthine Diuretics.—Theocine is said to be the most powerful of the [illegible]

with ethylenediamine Reference to its use is made under the heading of Refractory Congestive Failure (p. 545).

Vitamins.—Cardiovascular disturbances attributable to vitamin deficiencies occur commonly in chronic alcoholism and in non-alcoholic subjects as a result of an unbalanced diet Beriberi in the wet form is the classic example, but minor degrees of vitamin deficiency occur throughout the general population in non-tropical countries It is for this reason that vitamin concentrates have been advocated in the treatment of chronic congestive failure in which as a result of a poor diet and prolonged portal congestion low-grade deficiency states may complicate and aggravate the situation.

Thiamine (aneurine) has diuretic properties and may be administered parenterally to ensure absorption in daily doses of 5 to 25 mg. or more. Vitamin C has been shown to be of value in similar circumstances and may be administered to patients with congestive failure in tablet form by mouth as ascorbic acid (50 to 300 mg) three or four times a day It may also be given parenterally in doses of 100 to 500 mg , but this is rarely necessary.

Mechanical Procedures

Venesection.—Of mechanical methods of treatment one of the most important is the old remedy of venesection The precise indications for its employment are difficult to determine Most benefit is likely to accrue from this method when both the arterial and venous blood pressures are raised, though there are exceptions even to this rule. It is contra-indicated in the presence of anæmia or a low arterial blood pressure When the liver is acutely engorged, painful or pulsating, and there is much cyanosis and pulmonary œdema, the procedure may generally be used with considerable benefit. Venesection in such circumstances unloads the right side of the heart In urgent cases it is only necessary to incise an engorged vein at the region of the elbow and allow the blood to spurt A needle of as large a bore as can be [illegible]

and often appears to permit an improved response to digitalis therapy. The method is much less efficacious in long-standing cases of heart failure when, after months or years, cirrhotic changes have occurred in the liver and other organs.

Paracentesis.—Hydrothorax or ascites seldom warrant mechanical interference until a fair trial has been made with other methods of treatment. Fluid at the base of either lung is a common occurrence in congestive failure, and may on occasions be bilateral. If it is resistant to treatment and the chest more than half full, then a two-way syringe is a convenient method of withdrawing it. At the conclusion of the paracentesis the injection into the peritoneal or pleural cavity of 1 to 2 ml. mersalyl suitably diluted is a procedure which has been practised, but has little to recommend it, as the mercurial is probably not absorbed any more freely from either cavity than after its intramuscular injection. The mechanical removal of large quantities of fluid from either the thorax or peritoneum often appears to expedite recovery.

SYMPTOMATIC TREATMENT

Cough and Pain.—The measures, already described are in themselves usually sufficient to ease the patient's discomfort, but from time to time other symptoms arise for which relief is sought. Amongst these, cough, attributable to the pulmonary congestion, is often trying to the patient, particularly when it occurs in repeated paroxysms, and tends to interfere with sleep. As congestion subsides under the influence of digitalis and diuretics, bouts of coughing as a [illegible] necessary, is a suitable remedy. On the other hand, chronic bronchitis with an asthmatic element occasionally complicates congestive heart failure, and in these [illegible] hæmoptysis which commonly accompanies the infarct may cause a good deal of mental anxiety From both points of view, morphine is the best drug to employ in the first instance · later the pain may be soothed by hot applications in the form of fomentations or kaolin poultices.

Oxygen Therapy.—This as a rule has only a limited application in the treatment of circulatory disease. It will do nothing to correct cyanosis which results from circulatory stasis in the periphery. On the other hand, pulmonary congestion and œdema of the alveolar walls may interfere with the normal oxygenation of hæmoglobin in the lung capillaries. This lends itself to treatment if it is possible to increase the partial pressure of oxygen in the lung alveoli. Clearly, both factors, pulmonary congestion and peripheral stasis, frequently coexist. The final test of the value of oxygen is its effect on the patient. If the cyanosis promptly disappears when oxygen is inhaled in sufficient quantity, then the treatment can usually be continued with benefit. It is only worth while

[1] Brompton Mixture —

℞	Solution of Morphine Hydrochloride .	6 ml (1½ fl dr.)
	Dilute Hydrocyanic Acid . .	2 ml (½ fl dr)
	Syrup of Tolu . .	30 ml (1 fl. oz.)
	Acid Infusion of Roses	180 ml (6 fl. oz.)

persevering with oxygen therapy if the patient derives real benefit and ca tolerate comfortably the method of administration. Dyspnœa is often apparentl lessened by its use. The technical details of oxygen administration are describe on p. 880.

REFRACTORY CONGESTIVE FAILURE

From time to time patients are encountered who respond so poorly or not at all to all the usual measures, in particular to digitalis and mercurial diuretics, that congestive failure in greater or less degree persists in a chronic form for many months. The patient is bedridden, "water-logged" and virtually helpless. To this minority the term refractory congestive failure is applied.

Their further treatment poses a number of considerations. It is first desirable to ensure in the low-output groups that adequate digitalization has been achieved and maintained. A second step is to exclude the "salt-depletion syndrome" (p. 105), in which lowering of the plasma electrolytes below a critical level is apparently accompanied by further deterioration in renal function with consequent retention of corresponding amounts of water and simultaneous aggravation of the accumulated œdema. In these circumstances treatment consists in countermanding mercurials and encouraging an increased salt intake. By replacing the impoverished sodium of the tissue fluids a satisfactory diuresis may be restored and symptoms eased correspondingly.

Of the drugs employed to enhance diuretic remedies, ammonium chloride is the most popular. It supplies the body fluids with the chloride necessary for the maintenance of diuresis and it also acts as an acidifying agent. The latter property apparently influences the osmotic pressure of the tissue fluids and alters the water-binding properties of the proteins, thus facilitating the removal of extracellular water.

Ammonium chloride has an objectionable flavour and is best prescribed in cachets or enteric-coated tablets, each 0.5 g. (7½ gr.), but if these prove difficult to swallow an attempt may be made to disguise the taste by adding liquid extract of liquorice or syrup of orange to the mixture, as in the following prescription:

℞	Ammonium Chloride	2 g. (30 gr.)
	Liquid Extract of Liquorice	2 ml. (30 min.)
	Spirits of Chloroform	0.5 ml. (8 min.)
	Water to	15 ml. (½ fl. oz.)

Sig. Tablespoonful as directed.

effective method of administration is to restrict the employment of nonium chloride to the twenty-four-hour period immediately preceding the salyl injection. To allow the patient to become adjusted to this routine it is wise to commence with a single dose of ammonium chloride, 1 to 2 g. o 30 gr.), on the first day on which it is used. The quantity can be doubled e second occasion and ultimately the dose increased to a total of 6 or 8 g. on priate days if tolerance permits. It is apt to induce nausea and vomiting tolerance is acquired. By this means the response to mersalyl is often ciably enhanced.

mbined with a mercurial, aminophylline can on occasion produce spec- results. In addition to inhibiting tubular reabsorption, aminophylline es effective renal blood flow and glomerular filtration. It also temporarily

diagnosis The lethargy deepens, twitching movements of the hands and fore-arms are noted, and as coma advances a diagnosis of terminal uræmia is justified by the fatal outcome.

The cause is a profound disturbance of kidney function. A low urinary [illegible]

A watch should be kept on the urinary response to mercurial injections, the *blood nitrogen*, the *blood sodium* and chloride levels, and the course of the body-weight chart. Dangers are most apt to threaten when the low sodium diet is combined with mercurial injections. It is then that a weekly record of the blood urea provides a useful guide to renal function, increasing nitrogen retention [illegible] -vented by restor- [illegible] fortnight, or the [illegible] -weekly intervals instead of daily as is sometimes done when the patient's response is sluggish In fact, less energetic therapeutics for the patient with congestive failure may permit his recovery.

In the actual emergency of the uræmia-like state, symptomatic relief may be obtained by an infusion of 25 g. or more of sodium chloride in 5 per cent. [illegible]

THE SYNDROMES OF ACUTE CONGESTIVE FAILURE

Acute Left-Ventricular Failure

(" *Cardiac Asthma* " *or Paroxysmal Nocturnal Dyspnœa*)

Reference has already been made to the nature of this serious and alarming disturbance in which the right ventricle continues for a time to pump more blood into the pulmonary circuit than the left ventricle is capable of accepting. [illegible] The patient is found sitting upright [illegible] and drenched in a cold [illegible] They consist of bouts of orthopnœa and restlessness with or without a tickling paroxysmal cough. [illegible] It is common in middle- [illegible] ion or [illegible] ctims *of a tight mitral stenosis In these circumstances* the attacks are sometimes described as acute left auricular failure. They are then the immediate result of over-exertion, which accounts for their liability to occur in pregnancy or after labour, whereas in the elderly difficulties commonly begin at night some hours after a strenuous day.

Many of the milder attacks subside spontaneously in an hour or two without drug therapy. Complete rest, a comfortable upright position in an arm-chair by the fire, quiet and reassurance, may be all that are required to relieve the

minor upset, but left-sided failure is a treacherous condition More serious symptoms call for active measures

the relief of cardiac gr.) by hypodermic stress has not been

appreciably eased. The heart should be promptly digitalized This is an occasion which justifies a full intravenous dose of a powerful glycoside. Either

intravenous use is not essential Within twenty minutes of the administration of either of these remedies distinct improvement should be evident The patient should not be left unattended until coughing and dyspnœa have ceased, and he has settled for sleep.

In *hospital practice*, when it is certain that acute left ventricular failure is the direct result of an exacerbation of hypertension and not of acute myocardial infarction, and when accurate records of blood pressure can be recorded at intervals of a few minutes, the slow intravenous injection of 4 mg of hexamethonium bromide or chloride at two-minute intervals until the blood-pressure readings begin to approach normal figures is a method of treatment of considerable value As the heart is released from the hypertensive load, pulmonary congestion subsides and symptoms are correspondingly eased Rapid digitalization can then be induced to prevent a relapse and arrangements made for a continuation of control of the blood pressure by oral medication

1 5 mg. digoxin) is the first step Little reliance should be placed on atropine, 0 6 mg. ($\frac{1}{100}$ gr.) hypodermically or intravenously, for, with the appearance of the characteristic sputum, a venesection will be required. This is best done by

one of the antecubital veins In less urgent cases a bloodless phlebotomy can be performed by the application of blood-pressure cuffs, rubber tubing, tourniquets, or towels, tight enough to retard the venous return but not obliter-

stimulant, and is contra-indicated in both congestive and anginal failure. It increases cardiac work, but in small doses the element of bronchospasm in the production of cardiac asthma may be eased by its use, and possibly the tendency

dose of 15 to 20 mg. ($\frac{1}{4}$ to $\frac{1}{3}$ gr.) should be repeated without hesitation in an hour should pain be unrelieved, *and further doses are likely to be required* during the first twenty-four to forty-eight hours. For the later doses oral administration of the 15 mg. ($\frac{1}{4}$ gr.) tablets at the hands of the attendant, under medical direction, is satisfactory. A limit is set to dosage only by the development of general toxic symptoms, for the drug exerts no deleterious effect on the heart. Morphine is invaluable because it relieves pain and abolishes anxiety: adequate

ever, these symptoms also occur as after-effects of morphine—especially in women. It is therefore important accurately to assess the significance of nausea and vomiting in these circumstances.

Anticoagulants.—*Heparin and drugs of the coumarin group have been* used in the treatment of coronary thrombosis for some years, and there is a fair measure of agreement as to their value, though less is known as to the precise mode of action.

In the group of patients in whom persistent or recurrent pain and prolonged shock indicate a spreading thrombosis, limitation of the process by an anti-
…indicated when the electrocardiogram
" involvement of the ventricular
formation and high risk of sub-
ithout complications, the routine
administration of anticoagulants is of value, and a lower mortality has been claimed particularly in the large group of male patients who, prior to the onset of infarction, have suffered little or no disability.

Attempts have been made to select patients for anticoagulant treatment by assessment at the outset as "good risk" or "poor risk" cases on a clinical basis. Prolonged pain, severe shock, early failure, etc., on the one hand, and transient pain, maintained blood pressure and colour, minimal EGG changes on the other, influence this segregation. It has been shown that *as a group* the "good risk" cases show relatively little benefit from anticoagulant treatment as compared with controls of comparable severity. On the other hand, the spread or recurrence of thrombosis may overnight convert an initial "good risk" individual case into a desperately ill patient, and there is no certain method of predicting which particular patients will suffer this unfortunate deterioration. For this reason, the writer does not advocate or practise such selection for anticoagulant treatment, but gives all patients with clinically diagnosed coronary occlusion the protection of anticoagulant drugs. The duration of treatment and rest are naturally profoundly influenced by the clinical assessment of the severity and extent of the damage to the heart muscle.

…experience, proved
lelayed and persist-
fects, together with
'ise, have led to the
in use: ethyl bis-
coumacetate (Tromexan) and phenindione (Dindevan) These have similar anticoagulant properties, but are much safer in use, since their actions are transient and readily controlled. They are, however, emphatically drugs for use

only in hospital No one should embark on anticoagulant therapy unless he is prepared to keep his patient under close clinical observation for signs of over-

disasters have occurred in cerebrovascular accidents complicating the coronary

It is usual to administer heparin for forty-eight hours after admission to

thrombosis, and should not be administered, particularly as shock is usually

istration of

w days, is

ve failure is

lessen the

risk of ventricular fibrillation, and in cases where there seems to be likelihood of

Shock in cases of coronary occlusion varies markedly in degree Treatment on symptomatic lines by warmth, etc., should be instituted, and may suffice in the milder cases Profound shock develops in a minority of cases with massive infarcts, and in general is associated with a grave prognosis and a rather intractable course Some patients, however, do respond to treatment, and may go on to a smooth convalescence, so that every effort should be made in all cases It is in these severely shocked patients that oxygen administration is of conspicuous value To be effective, the gas should be given in high concentration (say 6 to 7 litres per minute) by B.L.B. mask continuously for many hours.

Large intravenous infusions carry a serious hazard from overloading a damaged myocardium, and adrenaline, ephedrine and pituitary extracts are contra-indicated on account of their cardiac actions The recently introduced noradrenaline (Levophed) has a known marked vasoconstrictor action without the cardiac accelerator and augmentor actions of adrenaline, and is of some value. It is given intravenously by drip in a concentration of 2 mg per litre, at a rate of

into the rectum, followed by a saline enema in the morning, is a safe and effective method of opening the bowels.

Various complications may arise during the first few days or weeks, and may demand treatment.
along the usual lines.
fibrillation is present,
days only after weighing the risks of giving the drug or, on the other hand, of withholding it. Diuretics such as organic mercurials are of value, and venesection may afford relief in cases with great venous engorgement. If dyspnœa is

treatment.

The occurrence of embolism is an ever present risk, favoured by exertion but not entirely eliminated by rest. Prolonged recumbency, in fact, by inducing thrombosis in the leg veins, may lead to pulmonary embolism. Its incidence, from either source (mural thrombus or phlebothrombosis) is markedly reduced by efficient anticoagulant therapy (see p. 92). Otherwise the treatment of cases where embolism has occurred is on symptomatic lines, and absolute rest is secured by morphine From the nature of the cases surgical intervention is not generally practicable where arterial embolism of main limb vessels has occurred.

Recurrence of pain may occur at any time, and even slight persistent pain recurring over a period of days is disquieting. Relapse can occur, though less commonly, in cases treated with anticoagulants. In this event the potency of the anticoagulant should be checked at once, and the dose increased if necessary. Prolongation of the period of rest in bed may be justifiable

The actual duration of confinement to bed varies with the severity of the case. Where intense and prolonged pain, profound shock and the electrocardio- ... indicate an extensive lesion involving

failure), and these are increased by exertion. After six weeks or so these risks ... On the ... return to activity in two to three weeks. The ... in bed for meals and ... weeks after the infarct, ... *hours daily.* The

the prescribed period, part
few days after the attack.
patients who have had no pain. Explanation that the heart has been damaged, and that it takes some weeks to heal properly, will usually render the patient amenable to discipline. But one must be careful not to induce a state of undue ... of mind may result,

gloom on the part of the attending physician is not only inhuman but is not justifiable. The risks to be run during convalescence must be kept in mind by the doctor, but must not be used as a bogey to frighten a patient into submission. And it should be realized that not the least of the patient's risks is that of developing a cardiac neurosis which may be more crippling than his organic lesion.

Patients who have suffered an attack of coronary thrombosis, whether or not residual effort angina persists, should in their after-care be treated on the same lines as the subjects of effort angina (see below).

Angina of Effort

Treatment of Attacks.—It is unusual for a patient to be seen by his doctor while actually in the throes of effort angina. The attacks are of short duration and occur while the patient is about his daily business, and even if a medical man is summoned the pain is likely to have abated spontaneously before he reaches the patient. A patient whose pain has lasted without intermission for half an hour or more in spite of resting should probably be regarded as a case of coronary thrombosis and treated as such In such a patient the prompt use of heparin may forestall a massive thrombosis. The same applies to patients previously free from angina or suffering from attacks of only moderate severity who suddenly develop attacks of great frequency on slight exertion they should [illegible]

later to small scars in the myocardium

The patient who is habitually seized with præcordial pain while walking [illegible]

or resistant cases one or other of the quickly acting nitrites can usually be relied on to afford speedy relief, and the subjects of effort angina frequently carry such preparations in readiness for emergency use. The traditional remedy is amyl nitrite, carried in small capsules or " perles " containing 0·2 to 0 3 ml (3 to 5 min.) These are individually encased in fabric covers, permitting them to be broken in the fingers without fear of cuts from broken glass. The broken ampoule is held to the mouth and a few deep breaths taken with the mouth open The *action is speedy and relief from pain is frequently achieved* The vasodilator action produces flushing and often headache or giddiness, and the patient may hesitate to use the drug on the grounds that such discomforts are harder to bear than a mild attack of pain. In severe attacks, of course, the benefits from nitrite far outweigh the unpleasant side-actions. Amyl nitrite fails to afford [illegible]

Both amyl nitrite and nitroglycerine have a brief action, but longer acting analogues are now available, such as pentaerythritol tetranitrate (see p 557) Nitroglycerine is dispensed in chocolate-coated tablets containing the desired dose, together with milk-sugar to make up a convenient bulk. The dose

required to abort an attack varies in different cases, but it is convenient to prescribe the B.P. tablets of glyceryl trinitrate containing 0·5 mg. ($\frac{1}{120}$ gr.), and to adjust the number of tablets taken to secure the appropriate dose. While relief may follow the taking of as little as 0·25 mg. ($\frac{1}{240}$ gr.), 0·5 mg. ($\frac{1}{120}$ gr.) is usually required and sometimes 1 mg. ($\frac{1}{60}$ gr.) or even exceptionally 2 mg. ($\frac{1}{30}$ gr.) may be necessary. It is important to instruct the patient to chew and suck the tablets, as absorption has been proved to be most rapid from the buccal mucous membrane. As this substance deteriorates when kept in contact with air for long periods, only small quantities of tablets should be prescribed at a time. Tablets stored in bulk should be kept in full bottles sealed with paraffin wax.

If nitrites are not available and the attack is severe and prolonged, alcohol, as whisky or brandy, may afford relief. The use of alcohol even occasionally is not, however, to be recommended, in view of the obvious danger of habit formation. Morphine likewise, which relieves the pain, is very undesirable in cases with chronic recurrent pain because of the risk of addiction.

After subsidence of the pain in an attack, many patients are able to resume walking or other activity where they left off, but should be warned that a slower pace than that which provoked the pain is to be adopted.

General Management.—The treatment of actual attacks of pain should be looked upon as a very minor part of the treatment of a case of coronary disease. Reduction in the number of attacks is of vastly greater importance, and a great deal can be done by wise management to achieve this end. Much more will be accomplished by regulation of the mode of life at work and at play, of habits regarding meals and the use of alcohol and tobacco, and by advice on other mundane matters than by the administration of drugs. It is a travesty of our therapeutic knowledge to make a diagnosis of effort angina and to send the patient away merely with a box of amyl nitrite " perles " and instructions to inhale one when the pain is felt.

A large proportion of patients are of the overweight, thick-set type, and in these reduction in weight is probably the most potent therapeutic measure. The loss of one or two stones of superfluous weight greatly eases the burden imposed on the heart, and frequently results in a striking improvement in the exercise tolerance without the use of drugs. The sufferer from angina should be encouraged to attain a weight slightly under that which is average for the height, age and sex. This can be achieved by simple dietetic restrictions, provided the co-operation of the patient is secured. A further dietetic point hinges on the well-known tendency of attacks to occur when exercise is taken soon after a meal. Heavy meals are certainly to be avoided, and a rest or short sleep after lunch or dinner may greatly reduce the frequency of attacks in some patients. Thyroid extract as a weight-reducing agent is to be avoided in anginal cases, in view of the increased cardiac load it imposes.

The family physician, from his knowledge of the patient's habits and mode of life, is best qualified to instruct him as to what to do and what to avoid in his [illegible] of cases occur in the active type of business [illegible] patient's [illegible] demands [illegible] in which sudden severe unaccustomed physical exertion (e.g. [illegible]) has immediately preceded the onset of coronary occlusion. The avoidance of business

worries, relegation of as much work as feasible to juniors, the giving up of committee work involving responsibility or the strain of meetings, etc , are all points requiring consideration. Physical effort can be reduced considerably by taking

days to a pleasant easygoing round, and so c
employed in heavy manual labour, or in
(postmen, rent collectors, shopkeepers, e

to the subjects of severe angina, because of the risk not only to themselves but to others—e.g drivers of locomotives, buses, etc., while the fitness of the patient to drive his car must be assessed, and constantly reviewed, by the doctor.

In any case, whatever other measures are taken to spare the heart, it is always possible to arrange that the patient can have at least eight hours' sleep each night, with, in addition, Saturday afternoon and Sunday in bed if required. At the outset of treatment in severe cases considerable improvement follows an initial period of two to three weeks' absolute rest in bed The relief may persist after return to activity, and the increased cardiac reserve is revealed in the amount of work required to provoke an attack Periodic spells of rest in bed are of value to many patients who otherwise have difficulty in securing enough rest.

the patient may suck one or two tablets of the B.P. preparation. Attacks produced regularly by climbing a flight of stairs may thus be prevented, or the strain of an important business meeting may be undertaken without discomfort. Many

etc) is an effective vasodilator in oral doses of 25 mg , but in many patients it produces nausea to a degree that precludes its use Another is pentaerythritol tetranitrate, which in doses of 20 to 60 mg twice or thrice daily often proves satisfactory in reducing attacks The ambulant patient who is using vasodilators to prevent attacks must be warned that they are intended to allow him to pursue his essential daily business at a very low level of energy expenditure, and are not to be taken with the object of allowing him to return to a more strenuous mode of life

The widely advertised vasodilators of tissue origin (muscle and pancreatic extracts, etc) are of little or no value in the treatment of angina. Drugs of the

transient and results from either extreme bradycardia, ventricular arrest or *ventricular fibrillation on the one hand*, or from an excessive ventricular rate as in the paroxysmal arrhythmias on the other. In either instance the symptoms are similar, and are due to cerebral anoxæmia. The prevention and treatment of the paroxysmal tachycardias, a potent cause of syncope in elderly people, are discussed on p. 599.

Stokes-Adams Seizures are syncopal attacks associated with a defect transient or permanent, in the conducting mechanism of the heart beat. In the majority of instances they can be prevented by the regular administration of ephedrine hydrochloride in doses sufficient to increase by a few beats per minute the slow idioventricular rate. For this purpose a dose of 30 mg. (½ gr.) of ephedrine by mouth in tablet form at either four- or eight-hour intervals may be sufficient. Larger doses may cause overstimulation and exhaustion of the ventricular centre. While ephedrine is the most reliable drug to use for this purpose it is not effective in every case, probably for the reason that the mechanism responsible for ventricular arrest varies in different individuals. Adrenaline, given by subcutaneous injection either as the B.P. preparation, or in oily solution which makes it slower in action, may be substituted for ephedrine, should the latter be ineffective. The proprietary preparation Adrenutol (adrenaline in oil) 1 to 2 ml. by intramuscular injection once or twice in twenty-four hours has the advantage of a more prolonged action. Atropine is of little value, but may be tried if ephedrine, adrenaline or Adrenutol fail.

Recovery from the actual Stokes-Adams attack usually occurs before any particular treatment can be prescribed. The ventricles resume their rhythm spontaneously. In the more severe attacks, as the circulation is in abeyance,

fine needle about 3 in. long attached to a syringe charged with 0 25 ml. adrenaline (1 : 1,000 solution) is inserted into the fourth left intercostal space about one finger-breadth from the sternal border. This site avoids the internal mammary artery and diminishes the likelihood of puncture of an underlying branch of a coronary artery or vein. The needle-point is inserted to a depth of 2 in. or more, and when the ventricular cavity is reached blood may be withdrawn into the syringe The injection is then made, but actually it is of little consequence if the adrenaline is deposited either in the myocardium or within the cavity of the ventricle. The resumption of ventricular contractions is as a rule so immedi-

Stokes-Adams seizures but also in the cardiac arrest of anæsthesia, electrocution and in anaphylactic shock. It may also be employed *in asphyxia neonatorum*, ... drowning. The intracardiac injection

...ot without danger. Only the urgency

...ich, fortunately, there is now ample

...Adams seizures follow each other in

rapid succession, the patient regaining *consciousness only to lapse* back again into

coma every few minutes, perhaps twenty or thirty attacks occurring in the course of an hour. The milder seizures may amount to no more than a transient giddiness, but others proceed to profound coma and clonic convulsions Here, again, ... utes of a subcutaneous injection
recurring,
is purpose
plished by

the risk of ventricular fibrillation.

Very occasionally Stokes-Adams seizures are due to this arrhythmia. ... necessarily a fatal condition, but if co-ordinate ... of
ro-
fect
has not proved of
... arrhythmia.
of Stokes-

Adams attacks when ventricular fibrillation ...

Collapse and Shock

(*Peripheral Failure*)

These terms, which are virtually interchangeable, are employed to denote an advanced degree of acute circulatory insufficiency, more gradual in its onset, more protracted in its course and of much more serious significance than the simple syncopes. There is no fundamental difference between "medical" collapse and "surgical" shock. The underlying mechanism, provoked by numerous agents, is similar in all three—syncope, collapse and shock. The amount of blood in *active* circulation is strikingly reduced.

Shock and collapse may occur relatively suddenly in the acute infections, notably influenzal pneumonia, in acute sepsis as in peritonitis; in the course ... delirium tremens; after spinal anæsthesia; profuse hæmorrhage; accompanying he heart, lungs and brain; after an

disorganized as a result, it is believed, ... of the arterioles. In the later stages either an associated dilatation or constriction of the arterioles. In the later stage there is capillary paresis and an alteration in the permeability of the walls of the finest vessels (Weiss). This has the important consequence of allowing the diffusion of plasma fluids into the adjacent tissue spaces. The circulating volume of blood is reduced as indicated by a rise in hæmoglobin percentage and ... Clinically the ashen-grey colour, the impaired mental ... the thready pulse, the cold perspiration and ... make a fairly characteristic syndrome.

... A horizontal or ...

As regards treatment, posture is of the first importance. A horizontal or sitting posture may have to be maintained in certain instances, but whenever

possible pillows should be withdrawn from beneath the head

generous amount of warmth, either in the form of numerous hot tins, or by the application of a "shock cage" in which heat is maintained by electric bulbs. Heat may be employed internally as well as externally by the provision of hot drinks either in the form of normal saline or as salty soup by the mouth, and by a *hot solution of glucose*, 5 per cent., in normal saline by the bowel if need be.

The correction of dehydration, relative or absolute, is particularly valuable in the acute circulatory failure of fever and in post-operative collapse, but con-

of a satisfactory circulatory volume can be brought about by a continuous intravenous saline drip. By this means 3 to 6 litres of fluid may be added to the circulation in the course of twenty-four hours or more. To the normal saline thus used various substances of value in the treatment of shock may be added; glucose, nikethamide and hydrocortisone may all serve a useful purpose.

In traumatic shock, with oozing of serum into and around crushed and

the intravenous-drip method, blood may be run into a vein at a rate of 100 to 200 ml. per hour, and this can be maintained for twelve or twenty-four hours or longer, depending on the patient's progress and general reaction. In assessing the situation, repeatec [illegible] ie. A systolic pressure falling below [illegible] indicates the necessity for further transfusion.

The demand for large quantities of blood at short notice has led to the establishment of blood "banks" from which stored and suitably typed blood

restoration of ... employed. For ease of transport, stability and for the opportunity it affords of using higher concentrations of plasma, dried human serum has many advantages. The serum from all blood groups is pooled, concentrated and dried by special methods. The reconstituted solution prepared immediately before infusion by adding a suitable quantity of non-pyrogenic sterile distilled water to the dried serum powder, can be administered with safety to all blood groups without preliminary typing. This method was used with success in the treatment

[illegible] pressure within the vessels in [illegible] the severer grades of shock, Best and his colleagues have suggested the employment of a solution of serum of four times the normal concentration in place of the usual solution of the serum powder or in place of whole-blood transfusion This modification of the

reconstituted serum for transfusion is still in the experimental stage. With concentrated solution the rate of transfusion should not exceed 50 ml. in ten

Synthetic plasma substitutes are coming into favour Of these the preparation dextran—a glucose polymer with a molecular weight approximating to that of albumen—has been widely used in Sweden in recent years. It is not pyrogenic, antigenic or toxic and is said to produce a prompt and lasting effect on blood pressure, benefit commonly persisting for three or four days. It is given in the usual way by intravenous drip as a 6 per cent. dextran solution in 0 9 per cent. sodium chloride.

Various drugs have been used in the treatment of shock Of these—at least on a theoretical basis—most justification can be claimed for the active principles of the suprarenal gland. Noradrenaline, extracted from the suprarenal medulla, in its actions on the cardiovascular system is almost exclusively a peripheral vasoconstrictor hormone It has been employed in recent years to maintain blood pressure during surgical operations and also in patients suffering from shock, particularly the serious grades of shock accompanying massive myocardial infarction. On account of its intense vasoconstrictor action, noradrenaline must be given well diluted in an intravenous infusion. The method, which requires for its control repeated blood-pressure readings by

the normal range. Adrenal cortical extract, by correcting abnormal capillary and cellular permeability, is believed to regulate the volume of the circulating fluid within the vascular system It is worthy of a more extended clinical trial in the treatment of shock and collapse than it has received to date It may be given in doses of 2 ml. every hour subcutaneously for an adult, or if added to transfusion fluid, then 2 to 4 ml to each litre would appear to be adequate dosage. The rate of flow of the infusion should be regulated according to the blood-pressure figures and the patient's response.

Anoxæmia has a detrimental effect on the central nervous system and aggravates all the features of shock. Oxygen therapy will be of value in those forms of anoxæmia in which œdema of the lung alveoli interferes with the

iod of

lation

by an action on the autonomic nervous system resulting in nausea and vomiting. As a general rule morphine is well tolerated in the early stages of shock and may be given in full doses if pain is at all severe After some hours, when the state

of collapse is more profound and the patient's general condition has deteriorated, then small doses are preferable. It must be borne in mind that the detrimental effect of severe pain is to be dreaded more than the reaction of the peripheral circulation to the drug.

Certain synthetic compounds such as nikethamide (pyridine carbonate of diethylamide) or leptazol (pentamethylenetetrazol), *when given parenterally*, have a reputation in the treatment of shock and are commonly used. It is probable that any benefit which results depends on their central action as respiratory stimulants. The former is supplied in a 25 per cent. solution in 1 ml. ampoules, and the latter in a 10 per cent. solution also in similar ampoules. In circulatory collapse of vasomotor origin either of these drugs may be [illegible]

mouth. They are less effective in the presence of organic heart disease, but may be given a trial to counteract the minor degree of peripheral collapse inseparable *from full and repeated morphine administration, e.g. in the profound* shock of an acute myocardial infarction.

The ideal drug for the treatment of peripheral circulatory failure has not yet been found. Weiss has suggested that a chemical which exerts a constricting effect solely on the venules will be of particular benefit, whereas a substance which simultaneously induces constriction of the arterioles as well may further impair the blood supply to the tissues. A drug with such selective properties has yet to be demonstrated. Various vasopressor agents such as methylamphetamine hydrochloride (Methedrine) are under trial. Until further clinical research has differentiated more sharply the different varieties of shock and collapse, and until more specific remedies become available, appropriate treat- [illegible]

[illegible] requirements.

A. R. Gilchrist.

THE INFECTIONS

RHEUMATIC CARDITIS AND RHEUMATIC FEVER

[illegible] many [illegible] tis- [illegible] ugh [illegible] d a

life as "heart cases" on the twin bases of an attack of [illegible] doctor's wrong assessment of a functional murmur, the continuing stream of adult cardiac cripples attending our hospitals reveals the inadequacy of our methods of treatment of the primary infection. Figures such as those of Findlay, published in 1931, make melancholy reading. He found that of nearly 700 cases of rheumatic infection in childhood, only one-third escaped cardiac damage, while one-third died within ten years of the first infection and the remaining third became cardiac cripples to die in early adult life. Such was

the outlook for patients treated with the best available skill of that day, and there is little to show that our results today are much better. Sulphonamides, penicillin, cortisone and corticotrophin have all been tried and have in turn been found in greater or less degree disappointing. Rest in bed and the administration of sodium salicylate or soluble aspirin remain, at least in domiciliary practice, the mainstays of treatment

Penicillin.—The discovery of penicillin, with its powerful action on streptococcal infection, led promptly to its trial in rheumatic fever, in the genesis of which streptococcal infection so clearly plays a part. It was soon apparent that penicillin was without effect on the course of the disease, and its use was abandoned. Recently, however, it has been re-introduced not to treat rheumatic fever but to deal with residual tonsillar streptococcal infection It is common practice today, for example, to give a short intensive course of soluble penicillin at the beginning of treatment, and to continue throughout the patient's stay in hospital and after discharge, with one of the long-acting preparations (e g. phenoxymethyl penicillin by mouth). Such treatment is given along with salicylate or other anti-rheumatic drug.

Cortisone.—In some patients with severe pancarditis cortisone has in the writer's experience produced dramatic improvement, leading not only to disappearance of fever and arthritis but to rapid resolution of the cardiac affection, improvements which have been maintained. In other cases, however, the hormone has signally failed to influence the condition, and there seems to be no means of predicting which patients will respond and which will not In any event, treatment must be controlled by frequent estimations of sodium and potassium levels in the blood, since the drug profoundly influences electrolyte balance and may produce œdema or even precipitate congestive failure. The other recognized side-actions have not proved troublesome in the relatively short courses required in acute carditis. One's experience, however, has confirmed that cortisone treatment can only be carried out in hospital with full laboratory facilities for control and under the guidance of an experienced physician. Though now available freely in practice, it is well to reserve its use for acute cases under institutional care. At the same time the author believes that in cortisone we have a drug which can on occasion produce effects of altogether a different order from those of other lines of treatment.

Rest.—The child who develops acute or subacute rheumatism should be confined to bed for a prolonged period. Good nursing is essential, and during the presence of active carditis the patient should not be expected or allowed to do anything for himself The achievement of complete physical rest in young children without acute symptoms may present considerable difficulty, but confinement to bed should be maintained even although the child is moving about freely in bed, for to allow such a child up increases greatly the demands made on the heart and circulation. During the period of fever, with its accompanying profuse perspiration, careful toilet of the skin is necessary and will lessen the [illegible]

the fever and arthritis Recent work on its mode of action, however, suggests that it may produce its effects through the pituitary-adrenal system, much like cortisone and corticotrophin. There is also evidence (Coburn Reid) that when

the blood salicylate level is kept steadily between 30 and 40 mg. per 100 ml., not only are the fever and arthritis abolished but the B.S.R. returns speedily to normal and the duration of the disease is shortened. Such chemical blood tests, which can be done with simple side-room equipment, are a valuable guide to adequate dosage.

If the condition is to be treated in domiciliary practice and blood salicylate levels cannot be estimated, the drug must be given in doses sufficient to produce the symptoms of mild salicylate intoxication. So-called drug resistance is in *many cases due to under-dosage. The daily dose required to produce " satura-*

etc.). In general, for an adult, doses of 1·5 to 2 g. (20 to 30 gr.) two- or three-hourly will be required, a total of 12 g. (200 gr.) per day being commonly sufficient. In children the effective daily dose varies from 4 to 8 g. (60 to 120 gr.) per day, according to age. The old practice of giving sodium salicylate with

before use. Dosage again has to be pushed so far as the tolerance of the patient permits, or until gastric symptoms prove a bar to further increase. Sodium gentisate, a substance closely allied to salicylate, in doses of 1 g. (15 gr.) four-hourly, appears to have similar therapeutic actions with less toxic effects. The intravenous administration of salicylate, formerly advocated by some and recently revived, has not been shown to possess appreciable advantages over oral

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done within a few days at most from the start of treatment. The drug should not, however, be entirely discontinued, but should be administered in smaller

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increased.

Local Treatment for the affected joints should be simple. Wrapping the affected parts in cotton-wool and bandaging to secure rest generally suffice

now and then in adolescent patients. One has seen cases in young adults in whom unequivocal carditis has been associated with arthritis of small joints, of hands and mandible and where lasting deformity has resulted. The differen-

through the maximum range, short of causing pain, should therefore be performed daily as soon as the most acute symptoms subside, and immobilization during the rest of the day should be in the best orthopædic position should ankylosis occur in spite of attempts to prevent it.

Focal Sepsis.—In many cases of rheumatic fever a focus of streptococcal infection in tonsils or upper respiratory tract remains active throughout the course of the disease. Penicillin, used as suggested above, has rendered it rare now for the physician to be faced with the desperate decision that formerly had now and then to be taken—whether to advise tonsillectomy to eradicate such a focus, with the known risk of provoking a severe and possibly fatal exacerbation. The risk of operation is such that every effort should be made to eradicate streptococci by antibiotics rather than hazard tonsillectomy Cover by antibiotics should be given before operations on teeth or tonsils in apparently quiescent rheumatic cases.

It is convenient to discuss here the advisability of tonsillectomy in children with a rheumatic infection in a quiescent state It appears that routine tonsillectomy of healthy children does not protect them against subsequent first attacks of rheumatic fever, and routine tonsillectomy after a first attack does not appreciably lessen the risk of recurrence of the rheumatism. It is probably wise to advise tonsillectomy only when the local condition is such as would demand operation in a non-rheumatic case, and then to choose the time for operation with great care.

Duration of Rest.—The question of how long a patient with rheumatic carditis is to be kept in bed is not easily answered No hard-and-fast time limit [illegible]

arthritis treated by a short period of rest followed by a relatively quick return to normal activity. On the other hand, in fully one-third of all cases with symptoms of the " Effort Syndrome " admitted to a special army centre for rehabilitation, the onset of the symptoms and of the disability could be traced to a doctor's warning to parents or patient that all forms of strenuous activity must be avoided. It is true that in all cases with clinical evidence of *active* carditis, rest in bed [illegible]

that moderate exercise is beneficial for the subjects of early valvular disease.

The criteria for determining quiescence of the endocardial inflammation must therefore be considered. A smouldering valvulitis may go on for many months, of sufficient intensity to produce eventual gross fibrosis, and yet with very little clinical upset. Pulse rate and temperature may be normal [illegible]

relation to the extent of the cardiac lesions Subcutaneous nodules when present indicate persistent rheumatic activity, but their absence does not exclude active carditis. The return of the blood sedimentation rate (B S R.) to normal is generally a guide to the cessation of activity, but is not infallible. The B.S R. is normal in the presence of congestive failure, but such cases are easily recognized,

and the question of allowing the patient up does not arise. Now and then a normal B S.R. persists in a patient in whom failure is absent while other evidence of carditis is patent. Conversely, a raised B.S R. naturally does not necessarily

a severe acute pan-carditis, which may progress to end fatally. The handling of such a case can be as sad a task as any that a doctor has to face; ordinary measures fail to arrest or even retard the disease, and treatment has hitherto largely been symptomatic. In such fulminating cases cortisone and corticotrophin have on occasion proved valuable, but in a proportion of cases these drugs, too, are impotent to stay the course of the disease.

Convalescence.—*When the period of complete bed rest is over, the return* to activity should be very gradual and should be carefully supervised. Any recrudescence of the rheumatic process should be met by a prompt return to complete rest.

The child who has weathered a rheumatic carditis is frequently sent for a short period to a convalescent home, and then returns to school and to full routine. This is unsatisfactory, and is probably responsible for much later disability. Convalescence should be protracted, and after the period in hospital *the child should be sent for at least some months, but ideally for a prolonged* period (six to eighteen months), to a convalescent home. In some parts of the country special homes have been established where adequate medical attention

cardiac involvement in whom some abatement or arrest of the mischief may be anticipated. Provision for the education of the children in such homes is essential.

After-Care.—On discharge from such an institution, or after long con-
the limitation
In cases with
h a prohibition
only on such strenuous exertions as competitive sports. Patients with gross *myocardial damage* and hypertrophy must, however, lead quiet, sedentary lives. Careful follow-up with periodic assessment of general health and cardiac
renewed rheumatic activity demands
erstandable that such solicitous
—a point always to be borne in
mind.
infection is important, and the
) continuously
exacerbations
of the rheumatic process, despite the ineffectiveness of these drugs in acute established relapses There is a slight risk of toxic side-effects, of which

(benzathine penicillin, B.P.) or the oral administration of 125 to 250 mg. of phenoxymethyl penicillin twice daily.

The choice of a future occupation should always be made under the guidance of the doctor. Instances of young adults with advanced cardiac lesions engaged in strenuous occupations are all too familiar, and would not occur if after-care

sedentary occupation which will not lead so soon to a cardiac breakdown

instrument making and watchmaking, etc) are remunerative, make little call on physical strength and maintain the patient's interest and independence. Often the journey to and from work or school, and the exposure to inclement weather involved, impose greater strain and risk of relapse than the actual physical strain of employment.

PERICARDITIS

A patient suffering from acute pericarditis, whatever the ætiology, should be nursed at complete rest in bed. In the common variety occurring in the course of an acute rheumatic carditis, the general lines of treatment are as described under that heading. In tuberculous cases the general measures are those appropriate to tuberculosis in general (see p 122) and streptomycin, isoniazid and PAS should be given in appropriate doses Cases which occur in association with pyogenic infections (hæmolytic streptococci, staphylococci,

residual disability

The relief of pain may call for treatment, though many cases suffer surprisingly little discomfort even in the presence of a gross friction rub. Mild

by cantharides blisters. This has many obvious drawbacks, and how far such treatment aided recovery is questionable. Relief from pain can be more easily

oppression. It is well recognized from experience in auscultation that pressure over the ribs increases the pain in pericarditis.

The development of a large effusion may embarrass the heart's action or interfere with respiration by causing partial collapse of the left lung. It is unusual for such symptoms to be severe enough to warrant aspiration of the pericardial effusion, but tapping must be carried out promptly with the appearance of the early signs of tamponade—rising venous pressure, onset of cyanosis, increasing dyspnœa and general uneasiness. Aspiration is also a routine diagnostic procedure when bacteriological examination of the fluid is necessary, or when empyema has to be excluded. For diagnosis the aspiration of a few millilitres of fluid will suffice, but for relief of pressure the aspiration of several hundred millilitres may be necessary. The technique of paracentesis is described on p. 874.

The discovery of pus in the pericardial sac is an indication for surgical intervention. Drainage may be established by open operation, with resection of ribs, or may be achieved by a closed method, by insertion of a tube into the sac through the soft tissue of an interspace and the maintenance of suction. Both methods yield good results, and the decision as to which to employ naturally lies with the surgeon.

In non-purulent cases recovery with absorption of the effusion is the rule, except in the cases of terminal acute pericarditis which occur in the last stages of Bright's disease and other cachectic conditions. Convalescence may be slow, and there is no efficient method of hastening the absorption of the fluid Repeated assessment of the size of the effusion and of the patient's general state will guide the physician in his decision as to management—when to allow the patient to move about in bed, when to allow him up, etc. Other patients, on recovery from the acute attack, may be allowed a fair amount of exercise, but should be re-examined from time to time during the ensuing years to exclude the development of other lesions or of chronic constrictive pericarditis. When pericarditis occurs as part of a polyserositis, supervision by physician and thoracic surgeon is desirable, for operation may be indicated at a stage before hard scar tissue or calcified deposits have formed

Chronic constrictive pericarditis is a surgical problem and is dealt with in the section on The Surgery of Cardiac Conditions (p. 605).

CIRCULATORY FAILURE IN ACUTE INFECTIONS

In the circulatory failure which occurs in acute infections such as lobar pneumonia, two factors are at work: central, due to failure of the poisoned heart muscle, and peripheral, due to dilatation of the poisoned small vessels. Of the two the peripheral failure is generally the more important. This is true even in diphtheria, where many of the deaths are due to peripheral failure, though in some cases the specific action of the toxin on the heart causes sudden (cardiac) death, often many days after the apparent subsidence of the maximum effects of the acute infection

The treatment of toxæmic circulatory failure really lies in its prevention by early and adequate treatment of the underlying infective condition. In diphtheria, for example, the timely administration of antitoxin reduces greatly the incidence of dangerous circulatory failure. In pneumonia also, early and efficient specific treatment with sulphonamides and penicillin will lessen the risk of later intractable toxæmic effects. In diseases where no specific treatment exists, or in which failure develops during a long illness, general measures to reduce toxæmia are employed to the best of our ability.

Once circulatory failure has developed, the prospects of successful treatment are not good. It is then too late for efficient specific therapy, and measures calculated to stimulate the heart or the peripheral vessels are disappointing. Of drugs which act on the heart, digitalis is the most widely employed. The use of digitalis in pneumonia, for example, was once traditional, though its value is now discredited The old controversy as to its value in this condition is hardly relevant in these days of efficient antibiotics.

Many other drugs which enjoy a reputation as cardiac stimulants, and which are widely used in conditions of toxæmic circulatory failure, are devoid of direct action on the heart. Strychnine appears to act solely on the central nervous system, and the various "diffusible stimulants" (nitrous spirits of ether, aromatic spirits of ammonia) act reflexly. None of these is a true cardiac "tonic", increasing the efficiency of the muscle. Adrenaline, it is true, has such an action, but it increases the tachycardia which is already a disquieting consequence of toxæmic failure, and is known to deplete the glycogen reserve of the heart muscle cells. In short, we do not possess any drug which can whip an exhausted heart to renewed activity or which can render the cells immune to circulating toxins

Peripheral vascular dilatation, as the principal element in the production of circulatory failure, more frequently demands treatment than the heart condition. Many drugs are available, adrenaline and noradrenaline, posterior pituitary extract, leptazol, nikethamide, intravenous hypertonic glucose, etc., and these are discussed in the section on Acute Circulatory Failure (p. 558) The results of their use in toxæmic states are by no means satisfactory. In fact, once such failure has developed, progression to a fatal issue is likely in spite of all therapy, unless the natural body processes succeed in overcoming the toxæmia, as in the crisis phenomenon of lobar pneumonia.

FOCAL SEPSIS IN RELATION TO HEART DISEASE

The exact role of focal septic infection in the production of heart disease and symptoms is somewhat uncertain. It is recognized that the *Streptococcus viridans* may gain access to the blood from foci, especially in the teeth, tonsils

of which physician and surgeon should be aware. This form of subacute bacterial endocarditis is generally highly resistant to the usual antibiotics. For this reason it is advisable to search for, and extirpate, such foci in all cases of congenital heart disease and in the subjects of rheumatic lesions. Of the latter, it is those with aortic disease or early mitral disease who are liable to develop endocarditis lenta, patients with long-standing mitral stenosis are rarely affected. The operation should be carried out after preliminary administration of protective doses of sulphonamides or penicillin.

It is also admitted that foci of sepsis may be of ætiological importance in cases with heart block of milder grades and in cases with obstinate extrasystolic irregularities. In such cases also, removal of the foci is desirable and is generally without risk if suitable prophylactic measures are taken by pre- and post-operative treatment with sulphonamides or penicillin (see p. 57).

The matter is not so simple, however, when symptoms or signs of gall-bladder disease are found in a case presenting clinical evidence of heart disease,

clinicians contend that chance association plays a part in the simultaneous occurrence of the two conditions. The subjects of cholecystitis are of the habitus

be kept in mind.

I. G. W. HILL.

CARDIOVASCULAR SYPHILIS

For the treatment of cardiovascular syphilis the reader is referred to the section on The Treatment of Syphilis, and particularly to p. 187.

BACTERIAL ENDOCARDITIS

Subacute Bacterial Endocarditis.—Until recently this disease was almost invariably fatal. Within the last seven years the outlook has been revolutionized by the employment of penicillin and other antibiotics in its treatment The collective investigations undertaken at various hospitals in Great Britain have yielded results which have exceeded all expectations. The facts suggest that a mortality rate exceeding 95 per cent in the pre-penicillin era has been replaced by a recovery rate of 75 per cent. or more amongst those patients thoroughly treated—surely the most remarkable of the achievements to be credited to penicillin therapy.

Early and effective treatment demands prompt diagnosis, which can nearly always be achieved by blood cultures. The α-hæmolytic streptococcus (*Strep. viridans*) is the commonest causal organism. Its resistance to penicillin and other antibiotics must be determined. As a measure of the sensitivity of the

organism the result can be expressed as a multiple of the resistance of the standard Oxford staphylococcus, which is taken as unity. The great majority of strains of streptococci recovered from the blood in cases of bacterial endocarditis have a resistance between one-quarter and twice that of the standard. Extremes ranging from 20 times more sensitive to 300 times more resistant than the Oxford standard are encountered only rarely, but must be considered if penicillin dosage is to be adapted effectively to the causative organism and the patient's particular requirements.

In general, if the resistance of the infecting organism is found to be less than four times the Oxford standard, a dose of 2 million units per day will be required Fortunately, the great majority of strains of streptococci recovered from these patients are freely sensitive to penicillin and 2 million units daily will be adequate All the evidence indicates that if the infection is to be overcome and relapse avoided, the daily dose of penicillin must be large and the course of treatment prolonged to six weeks. Failures result from too short a course, irregular injections and too small a daily quantity (see Fig. 4) Four-hourly intramuscular injections without intermission for six weeks are irksome, unpleasant and even exhausting, but they have been proved to be the most effective and certain method of treatment so far known With the long-acting preparations of penicillin now available, minor modifications in the frequency of the injections are under trial, but no attempt should be made in the present state of our knowledge to reduce the length of the course of treatment or the total daily quantity Two million units per day for forty-two consecutive days is recommended as a standard method of treatment when the organism's sensitivity is within the usual limits This routine nearly always prevents relapses and offers a good chance of full recovery.

A guide to the efficacy of the doses employed is to be found in the response of the patient and in certain laboratory tests. Within a few days, if the quantity of [illegible] doubled or trebled As a further test of the efficacy of penicillin against an organism of high resistance, it may prove helpful to have the penicillin content of the blood estimated—the sample being collected immediately before the routine intramuscular injection of the drug. In this way a minimum blood concentration in units per ml can be determined and compared with the in vitro [illegible]

Infections associated with an organism of high penicillin resistance may be treated with penicillin combined with some other antibiotic to which the particular strain has been proved sensitive In these instances the tetracyclines have proved disappointing and much less reliable than the combination of streptomycin with penicillin. Streptomycin has been shown to increase the sensitivity of certain streptococci resistant to penicillin and hence the combination of the two antibiotics may prove much more effective than either alone. This combination

of which physician and surgeon should be aware This form of subacute bacterial endocarditis is generally highly resistant to the usual antibiotics. For this reason it is advisable to search for, and extirpate, such foci in all cases of congenital heart disease and in the subjects of rheumatic lesions. Of the latter, it is those with aortic disease or early mitral disease who are liable to develop endocarditis lenta; patients with long-standing mitral stenosis are rarely affected The operation should be carried out after preliminary administration of protective doses of sulphonamides or penicillin.

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clinicians contend that chance association plays a part in the simultaneous occurrence of the two conditions. The subjects of cholecystitis are of the habitus and age which favour arterial degeneration and its sequelæ of angina and myocardial failure. The evidence in favour of the so-called "gall-bladder heart" is thus not convincing, and operations for removal of the gall-bladder should be undertaken only when there are clear indications, apart from the cardiac condition, to justify the step. The high mortality which attends this operation in *patients with hypertension, obesity and impaired myocardial efficiency* should be kept in mind.

I. G. W. Hill.

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[illegible]

are recovered, then the dose of penicillin is obviously inadequate and should be doubled or trebled. As a further test of the efficacy of penicillin against an organism of high resistance, it may prove helpful to have the penicillin content of the blood estimated—the sample being collected immediately before the routine intramuscular injection of the drug. In this way a minimum blood

[illegible]

ten times that effective in the laboratory test

[illegible]

has the additional advantage that bulky intramuscular injections of penicillin, each of several million units, can often be avoided—the quantity of penicillin necessary being less when streptomycin is also in use. Streptomycin requires ...tibular nerve damage. A dose of 1 g. ... combined with penicillin in a daily ...s' course.

When after repeated attempts, no organism can be recovered from the blood even after prolonged incubation (for two to three weeks) and the disease is

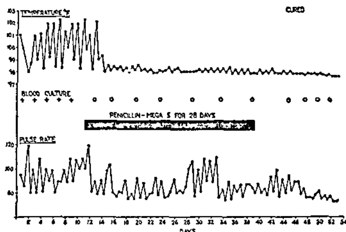


Fig 5

The temperature chart of a young woman 21 years of age suffering from subacute bacterial endocarditis engrafted on rheumatic mitral disease The immediate infection dated to the extraction of two teeth four weeks before admission to hospital, since when a swinging ...

regarded as inadequate for routine use.

The chart illustrates the lag in the temperature response to penicillin in this disease, two or three days commonly elapsing before the fever subsides

(From *Edin med. J*, 1948-49, p 25—*Medico-Chi*)

obviously active though in the "bacteria-free stage", treatment becomes empirical The prognosis in these patients is bad, the disease having run a ...

In the great majority of cases 2 million units daily for six weeks suffices to ...

usually observed within one month of completing the original course In arranging further treatment it is helpful to recover the organism and again have its resistance to antibiotics measured. In general the daily dose of penicillin

should be double the amount used on the previous occasion and the second course of penicillin lengthened to eight or even twelve weeks.

As has been pointed out above, most therapeutic experience in this disease has been based upon three- or four-hourly injections of penicillin maintained throughout the twenty-four hours. To avoid the necessity of such frequent needling, massive doses of penicillin in concentrated form are now coming into use. It appears that a single dose of 1 2 million units of a slow-acting preparation at 9 p.m. will provide an adequate blood concentration for a period of twelve hours, thus allowing an uninterrupted night's sleep. For example, benzathine [illegible] by a sustained concentration for twelve to eighteen hours. Intermittent three-hourly injections, each of 250,000 units, may then be resumed during the day, [illegible] million units of "All Purpose Penidural" may prove adequate Much depends on the response of the patient, and in such a serious disease there should be considerable hesitancy in modifying a routine now known to be life-saving.

When the infection is prolonged the patient's nutrition is likely to suffer [illegible] must be made to support the patient's strength by the provision of a generous high calorie diet Iron therapy is usually disappointing while the infection is active, but will help to restore the hæmoglobin level as the septicæmia is brought under control Transfusion is occasionally helpful, but must be used with caution on account of the danger of overloading the circulation and precipitating congestive heart failure.

Acute Bacterial (Ulcerative) Endocarditis.—Similar measures to those recommended above are to be employed in this disease. The prognosis has been vastly improved by the use of penicillin in the dosage employed in the subacute variety of the disease, and already cures are being reported in a condition which hitherto ended fatally in a matter of a few days

CONGENITAL HEART DISEASE

The remarkable advances made in the diagnosis and treatment of congenital heart disease in the last few years have aroused new interests in the care and management of these patients Symptoms in the usual acyanotic child are generally minimal or absent, though liable to appear suddenly as a result of a *respiratory infection or other complication* *The cyanotic child, frail, stunted* in growth and of poor physique, is usually handicapped to a greater degree. These children always need medical supervision and tactful handling. Their parents naturally look to the doctor not only for expert advice but also for [illegible]

abnormality predisposes to infective endarteritis of the pulmonary artery—an illness closely resembling bacterial endocarditis but complicated by recurrent pulmonary infarcts as a result of the detachment of vegetations springing from the wall of the artery opposite the orifice of the duct.

Closure of the ductus in youth prevents the development of this serious and commonly fatal disease, and avoids an uncertain invalidism which may provide in later years a basis for a cardiac neurosis or culminate in congestive failure. These late complications of the patent ductus can be forestalled by

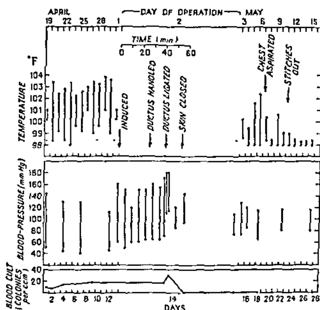


Fig 6

(From *Lancet*, 1947, ii, p. 267)

surgical occlusion, preferably before ten years of age when the child is relatively fit and tolerant of thoracic surgery.

Surgery can also be recommended in the presence of infective endarteritis, but the operative risks are probably ten times as great as in the non-infected patient. The associated septicæmia can be abolished in a matter of minutes by ligation of the ductus, and provided the infection has not run a prolonged ... and the *patient's condition* is reasonably good, surgery need not be ... septicæmia, ... icillin ... *tarted* therapy as outlined for subacute bacterial ... without delay. In these circumstances it is wise to ligate the ductus as *soon as*

the patient is judged fit to stand the operation, even before the completion of the six weeks' course of penicillin.

The results of surgical ligation are very satisfactory. The Gibson murmur is promptly abolished, the pulse pressure falls, and with the passage of time the pulmonary artery shrinks and the heart size is restored to normal. Accelerated bodily growth, better muscular tone, improved physique and a new sense of physical freedom are the rewards of successful surgery in this particular congenital abnormality.

Coarctation of the Aorta.—This curious obliterative stricture, situated as a rule just distal to the left subclavian artery, can usually be recognized in the child by comparing the femoral and carotid pulses, the former being weak or [illegible] lood [illegible] the [illegible] bout three-quarters of those affected dying by thirty years of age as a result of bacterial endocarditis, rupture of the aorta or as a consequence of the hypertensive state, intracranial bleeding being a common finding

The operative procedure which has been practised in recent years consists in the excision of the narrowed aortic segment with the reconstruction of the channel either by bringing together the remaining ends of the aortic tube and uniting them by a continuous everting silk suture drawing intima to intima or else by the insertion of a suitable aortic graft Where the narrowed aortic segment is very long, an aortic graft—being a human aortic segment collected and preserved after death from some aseptic case—proves very successful. The surgical mortality in experienced hands should not be more than [illegible]

The [illegible]

than [illegible]

older [illegible]

cut ends more difficult. In patients who have survived to the age of thirty, [illegible]

[illegible] in the interventricular septum. The net result is that venous blood from the right side of the heart enters the aorta [illegible]

[illegible] subclavian artery is anastomosed to the corresponding pulmonary artery, whereas in the Potts' operation a side-to-side anastomosis is made between the [illegible] Relief depends on the [illegible] difficulties will perhaps [illegible]

Unrelieved, 90 per cent. of these cyanotic patients die before twenty years of age. Both surgical procedures are formidable undertakings, but the poor prognosis taken with the almost miraculous improvement in physique and exercise tolerance justify the risk when the diagnosis is established with certainty. The operative mortality should be less than 20 per cent.

Pulmonary Stenosis.—In this condition the defect is restricted to either the pulmonary valve, which may be limited to an aperture only a few millimetres wide, or to the infundibulum of the right ventricle, where the fibrous obstruction situated below the valves takes various forms. Local surgery can relieve either form of stenosis. By the use of a special punch inserted through the incised ventricular wall the fibrous obstruction within the right ventricle can be resected or dilated, thereby permitting the onward flow of blood through the valve ring More commonly the defect takes the form of a diaphragm, formed by the stenosed valve, which requires to be cut transversely. Two cusps are thus formed which partially relieves the stenosis and reduces right ventricular pressure. Under hypothermia with the circulation arrested for two to four minutes, Swan has shown it possible to open the pulmonary artery and excise the stenosis. The results of this method are superior to those obtained by "blind" surgery. The degree of disability associated with this congenital flaw varies greatly and takes different forms, but the improvement directly attributable to surgery is striking and the experience gained to date is encouraging. The prospects are best in those submitted to valvulotomy before ten years of age.

Auricular Septal Defect.—Various procedures have been devised for the surgical closure of defects of the atrial septum. Direct access is possible under hypothermia with temporary arrest of the circulation. This permits rapid closure of the defect—a technique which has proved very successful in skilled hands.

HEART DISEASE IN RELATION TO PREGNANCY

Reference has already been made to the question of selecting a suitable occupation for those afflicted by heart disease in early life. Of all careers maternity may be the most strenuous, particularly in a working-class household, and therefore advice may be sought regarding the suitability of the cardiac patient for the risks and responsibilities of marriage. It is not within the [illegible]

in a short career is less likely to be able to provide adequate support for his dependants after his death. The woman with a cardiac lesion faces peculiar dangers, for the available evidence suggests that even surviving the immediate burdens imposed on her heart by successive pregnancies her days are likewise shortened. It should be realized, however, that the great majority of young women suffering from rheumatic heart disease are able, in reasonably good [illegible] the antenatal period, to bear one [illegible] nent, after which it may be con-

In no branch of cardiological practice is the ability to assess the degree of circulatory incapacity of greater consequence to the patient. Just as in the healthy woman minor degrees of cardiac embarrassment in the form of slight breathlessness and peripheral œdema often become apparent in the later months, [illegible]

is the development of [illegible]

reached. Labour in such circumstances is a burden which few will survive, and obstetrical interference undertaken in the presence of heart failure is the straw which breaks the camel's back. Pregnancy must be interrupted either in the earliest months in those likely to develop failure later, or, if it is allowed to proceed, adequate antenatal care and constant supervision must be made available throughout the pregnancy and labour conducted as expeditiously as possible

willingness to submit to perhaps prolonged periods of rest in bed, preferably in hospital, and her successful avoidance of upper respiratory infections and of the hypertensive toxæmias, either of which may impose an additional burden on the heart and precipitate congestive failure when otherwise unexpected Disturbances of cardiac rhythm have long been regarded with disfavour during pregnancy. Of these, auricular fibrillation is of ill-omen In the subject of rheumatic heart disease it indicates an advanced stage of the degenerative process and hence an increased liability to congestive heart failure.

It is recommended that when the patient first comes under observation she should be placed in the appropriate *functional grade* according to the following scale.

Grade 1 (formerly I): *Organic heart disease without limitation of physical activity* Ordinary activity causes no discomfort. Commonly the presence of organic heart disease has been recognized for the first time in the course of the routine ante-natal examination

Grade 2 (formerly II*a*) *Heart disease and slight limitation of physical activity.* They are comfortable at rest. When ordinary activity is undertaken, discomfort results in the form of undue fatigue, breathlessness or palpitation. Commonly these patients have come to avoid heavier household duties.

Grade 3 (formerly II*b*): *Distinct limitation of physical activity.* They are comfortable at rest, but distress in the form of fatigue or breathlessness is caused by less than ordinary activity. They commonly show a trace of

present even at rest. They present evidence of congestive heart failure in greater or less degree.

Patients in Grades 1 and 2 need give rise to little concern at any stage of pregnancy. For the most part these women do well and are able to go to term

abouts Hence the grade in relation to the duration of the gestation is of considerable importance. The lower in the scale the woman is, and the shorter the duration of her pregnancy, the worse is the outlook. Grade 3 is always a danger

signal and indicates the employment of energetic measures. Grade 4 spells disaster. These women are in grave peril.

The natural course of rheumatic heart disease, acquired on the average early in the second decade and terminating frequently in congestive failure fifteen or twenty years later, explains the *importance of age* in assessing the woman's capacity for pregnancy and labour. On the average the older the patient the

probable is the occurrence of serious incapacity.

If she has already borne a child, further guidance to the woman's capabilities readily becomes available. From her description of her symptoms her *previous experience* in a preceding pregnancy or pregnancies often enables fairly accurate assessment of her functional grade to be made retrospectively. Even in the milder grades (1 and 2) there is a definite downward tendency in a subsequent

second occasion.

Objects of Ante-Natal Supervision.—The main intention in the supervision of these patients is the adoption of measures designed to prevent the development of congestive heart failure—the commonest cause of death. All cardiac patients should be seen and graded within the first four months, or earlier. If major difficulties are to be avoided and catastrophies prevented at or about full-term, pregnancy should be terminated in the great majority of patients classified as Grade 3 and in all in Grade 4 by the sixteenth week, after which interruption becomes a major procedure associated with considerable risk for the patient with advanced heart disease By this means serious deterioration about the middle or end of pregnancy and death before or shortly after delivery can be avoided This aspect of the prevention of maternal deaths by early therapeutic abortion merits wider publicity. We might then be spared the tragedy of maternal deaths through neglect of simple measures appropriate to the first trimester.

The second step in the prevention of congestive failure during pregnancy is continued attention to the woman's general health. She should be seen either at home or at the ante-natal cardiac clinic every two or three weeks with a view to reassessment of her functional grade and with the object of ensuring that ... corrected.

...cipitate ...itis and ...ately be

confined to bed and given appropriate treatment.

The third step in the prevention of congestive failure is the provision of adequate rest and sleep. Women in Grade 2 should be advised to lie down for an hour or two each afternoon, have a long night's rest in bed and avoid fatigue There is probably no more important item in the care of these patients than the correction of insomnia, and for this purpose the hypnotic mixture (p 523) ... of heart failure is of great value Any patient

...ly ...in ...re

serious congestive failure, there is for these women, on whom danger threatens, no remedy superior to prolonged rest in bed, with the provision of adequate hours of sleep

Cæsarean Section.—The most difficult cases are those admitted to hospital

and dispersal of œdema. Improvement may be such as to justify a reclassification as Grade 2 or 3. Strict measures and absolute confinement to bed must be maintained for the remainder of the pregnancy in the hope that a natural vaginal delivery may be safely accomplished

If, on the other hand, energetic medical treatment given a fair trial fails to abolish completely the signs of congestive failure and the patient remains distressed, orthopnœic and œdematous, there is a natural temptation to empty the uterus artificially. The prognosis for mother and child is grave if the pregnancy is allowed to proceed, but even more grave if surgical intervention is undertaken in the presence of congestive failure In obstetric practice the working rule—"when in doubt don't interfere"—applies with particular emphasis in the management of these patients. The strain of the few days immediately following Cæsarean section is greater than after natural delivery, for labour in tragic circumstances is often made easier by Nature herself. Although the patient may survive the immediate effects of the laparotomy, an advance in the degree of congestive failure within a few days of delivery is usual and death common

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operative abdominal intervention. In severe cases, if labour is likely to be protracted and difficult owing to cervical rigidity or other obstetrical abnormality, there may be no alternative to Cæsarean section, but it reduces further the

to proceed

Mitral Valvulotomy.—Opinions are still divided regarding the indications for valvular surgery during pregnancy In general it is seldom justified, for experience teaches that the majority of women who have undergone valvulotomy while pregnant would have made equally good or better progress without operation had their medical supervision been adequate There is certainly much more justification for recommending surgery before than during pregnancy, even in the early weeks. Valvulotomy is not a procedure to recommend without most careful assessment. On the other hand, if serious dangers threaten—such as recurrent attacks of acute pulmonary œdema—and the response to medical measures is poor, then there may be no alternative to surgery. It should be understood that valvulotomy is more hazardous durin nancy than in the

non-pregnant state and that premature labour in the immediate post-operative period is common. As the serious cardiac complications of pregnancy can usually be anticipated and prevented by skilled supervision from the earliest weeks, the necessity for valvulotomy should not arise Only occasionally must it be employed, and then as a life-saving measure in a desperate situation.

Conduct of Labour.—In those patients who have been carefully supervised throughout pregnancy and whose circulatory efficiency has been well maintained, a successful delivery may be confidently *anticipated. As a general rule they* should be admitted to hospital or nursing home a few days—perhaps a week—before full term, provided with additional rest and sleep, and if necessary, digitalized rapidly. During labour a sedative is usually indicated, such as morphine, 15 mg. (¼ gr), and hyoscine hydrobromide, 0·5 mg. ($\frac{1}{120}$ gr), hypodermically. They should not be denied light anæsthesia, which they tolerate well. A protracted labour is to be avoided and the timely use of forceps is frequently desirable. In the puerperium a longer time spent in bed will be compensated for by better health in the following months.

HYPERTENSION

of much less favourable omen. On occasions both varieties are combined in greater or less degree.

In systolic hypertension, as its name implies, a high systolic reading is associated with a low or normal diastolic level A high pulse pressure is its characteristic feature. Systolic hypertension, which is the mechanical consequence of such conditions as aortic regurgitation, complete heart-block or an *arteriosclerotic and rigid aorta, is not in itself a disease entity nor is it an indica-*

frequently been confused.

Diastolic hypertension is the more serious variety For clinical purposes readings in excess of 100 mm. Hg. are regarded as outside the normal diastolic ... diastolic pressure is the product ... which the peripheral vascular ... the calibre of the arterioles, particularly of the splanchnic area, are reflected in gross alterations in the peripheral resistance and hence in the height of the diastolic pressure. Arteries. particularly the aorta and great vessels, become less distensible as the internal pressure rises, and hence for every increment in diastolic pressure, a corresponding gain in the systolic reading may be expected so long as the heart muscle ...

is one ... ening ...

hypertension is a major therapeutic problem, the successful solution of which would yield immense benefits amongst the middle-aged and elderly groups of the population.

Principles of Treatment.—The first principle in treatment is to be satisfied that an elevated diastolic pressure persists and is not merely the transient product of extraneous factors. An isolated reading, in a tense and nervous patient, unfamiliar with the method, apprehensive, and perhaps ill at ease in strange surroundings, is unreliable In such circumstances temporary elevations of pressure are com

twenty minutes'

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beyond normal limits.

The second step is to clarify the diagnosis A remediable cause must be

associated with the production of hypertension may be arranged in four main groups

(1) *Renal Diseases*—acute and chronic glomerular nephritis, chronic pyelonephritis, polycystic kidneys, hydronephrosis, renal calculus

(2) *Endocrine Disorders*—Cushing's syndrome, pregnancy toxæmias, phæochromocytoma.

(3) *Vascular Disorders* (affecting renal blood flow).—Congestive heart failure, periarteritis nodosa, coarctation of the aorta

(4) *Neurological Diseases.*—Certain brain tumours, bulbar poliomyelitis.

This classification is not intended to be exhaustive nor does it account for

ard to illustrate

For instance,

tumour, consists of total or subtotal adrenalectomy Excision of a coarctation with reconstitution of the aorta can promptly cure this particular variety of

adrenaline or noradrenaline, and the hypertension which occurs in either a paroxysmal or sustained form, can be completely relieved by the early operative removal of these tumours

A third principle in the medical care of these hypertensive people is to assess as accurately as possible the severity of the disability and adapt treatment accordingly It is as important not to overtreat, when symptoms are absent or trivial, as it is to employ an intensive routine when serious dangers threaten. The patient's safety depends upon the integrity of his arteriolar walls. To gauge his vascular state as a whole and thereby arrange treatment appropriate to the individual, information of the greatest importance is obtained by direct inspection of the retinæ. Simple studies of renal concentrating power, heart size and lability of the blood pressure are valuable aids in the assessment of the extent

and severity of the arterial disease, but are subsidiary to ophthalmoscopic examination.

Retinal Grading.—On the basis of the retinal appearances, one of four grades of hypertensive vascular damage can be determined for each patient. The table given below, constructed from the prognostic studies of Wagener and Keith on the course of essential hypertension, provides a basis for the adaptation of treatment to the severity of the vascular disease. This is a more satisfactory approach to therapy than the two alternatives customarily offered by dividing essential hypertension into its benign and malignant forms—both terms being unjustified and misleading. Grades 1, 2 and 3 are commonly included in the term "benign". Grade 4 is known as "malignant" hypertension. Broadly speaking, Grades 1 and 2 may be regarded as mild, Grade 3 as moderately severe, and Grade 4 as very severe or malignant.

	Grade 1	*Grade 2*	*Grade 3*	*Grade 4*
Symptoms	None to slight	Slight Morning headache Vertigo	Moderate Frequent headaches Fatigue Dyspnœa Nocturia	Severe Intense headaches Weakness Loss of weight Dyspnœa Confusion
Blood pressure	150/100-200/120	180/100-270/130	180/110-280/140	240/130-300/180
Retinæ	Minimal arterial narrowing	Definite sclerosis Arteriovenous compression No retinitis	As in Grade 2 with either exudates, star figures, cottonwool patches or hæmorrhages. Definite retinitis	Papillœdema, with or without Grade 3 changes Advanced retinitis usual
Renal function	Normal	Satisfactory; faint trace of albumen	Impaired; albumen with casts and R.B.C.	Impaired, as in Grade 3, but progressively deteriorating
3-year mortality rates	20 per cent	35 per cent	75 per cent	95 per cent

The retinal appearances provide a measure of the intensity of the hyper-
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is therefore the basic factor in determining suitable treatment. Account must also be taken of the age of the patient, more vigorous methods being justified in younger people than in the elderly, whose arteries are less resilient. Degenerative changes in vital organs may be so advanced as to debar any hope of successful

therapy. This applies more particularly to elderly people in whom a prompt reduction in blood pressure may prove harmful, if not fatal

Grade 1 or 2.—Most of these patients are over forty-five years of age. They require advice regarding their way of living and the day's routine. Long hours of work, domestic anxieties, emotional strain, the frustrations of modern business, the recurrent distractions of minor affairs, are aspects which may be considered with the patient, the doctor advising such restrictions as will allow of a definite routine without the production of further embarrassments If economic circumstances allow, a prolonged rest or leave of absence from work for three or four weeks may prove a desirable step The resolution of emotional conflicts with the adoption of a calm, philosophic outlook on life and its problems can do much to reduce the wear and tear on the circulatory system There are those who only after many years of elevated pressure begin to experience disagreeable symptoms. It is often found that they have been protected through their working years by regular habits, long hours of sleep, the short rest at midday, the quiet week-end, the protracted holiday, and perhaps, above all, by the cultivation of the placid temperament. The lesson to be learned from this is that by adapting the daily routine to the blood pressure, and thus keeping symptoms in abeyance, much good can be accomplished over a long period of time in middle-aged and elderly people without the use of active remedies, provided always that the emotional make-up of the patient is tempered by confidence.

By his manner, attitude and general demeanour, supplemented by a simple explanation of the facts, the doctor can do much to allay anxiety. As a general rule these patients require reassurance Their fears of high blood pressure should be countered at the earliest opportunity with the explanation that the condition is known to exist for many years and may even subside spontaneously without either serious embarrassment or permanent crippling It is fortunate that the great majority respond to simple psychological treatment of this nature. The doctor who naturally inspires confidence is best able to handle hypertensive patients, who usually prefer to be under the protective care and understanding of a sympathetic but enthusiastic adviser Relief from emotional tension is an important therapeutic step, and the doctor should aim to establish confidence and banish anxiety at his first contact with his patient Only exceptionally is it necessary with over-confident people to emphasize the dangers or issue a warning.

To the patient of inquiring mind it is often useful at the outset to explain that blood-pressure readings may fluctuate widely from time to time without much significance. He should know that the state of his artery wall is much more important than the pressure and that the level of the mercury seldom correlates with well-being. Unless it be a matter of reassuring the over-anxious, there is little to be gained by offering the patient either real or fictitious blood-pressure figures. In fact, the physician's endeavour in the majority of his hypertensive patients past middle-life is to prevent a further rise in the diastolic level and thereby reduce the rate of wear and tear.

Diet.—One of the most successful measures in the care of the middle-aged patient is the correction of obesity The prescription of an exact diet of 1,500, 1,200 or 1,000 Cals. will ease the burden on the heart and circulation (see p. 324) The weight will fall without much alteration in the diastolic pressure, but the relief of symptoms is often striking and the improved sense of well-being greatly appreciated A loss at a rate of 0.5 to 1.0 kg. (1 to 2 lb.) each week is sufficient. Consequently, according to his excess weight, many weeks of steady

perseverance may be required. Weekly weighings are a good guide to progress and are certainly worthy of more attention on the part of the patient than the blood-pressure readings

[illegible]

digestions, and the colour of the meat is no bar to their enjoyment of it.

Drugs—In the absence of renal damage, a small dose of calomel followed by a gentle saline purge has much to recommend it. When emotional tension runs high and there are obvious nervous influences at work, a small dose of phenobarbitone or chloral hydrate, once or twice daily, are useful remedies. Either chloral hydrate, 0 3 g (5 gr.), in a simple mixture in the forenoon and again in the evening, or a tablet of phenobarbitone, 30 to 60 mg (½ to 1 gr), may be ordered.

Rauwolfia serpentina has proved useful by itself in the treatment of the [illegible]

Many preparations are available. The refined whole root (e.g. Raudixin, in 50 mg. tablets, 3 to 8 daily), the mixed alkaloids (e.g Rauwiloid, 2 to 4 mg. thrice daily) or the single alkaloid (e.g reserpine, 0 25 mg. thrice daily) may be employed with advantage for long periods and without ill-effects. Full benefit is not obtained from this drug until it has been in use for two or three weeks. Few disagreeable side-effects, apart from nasal congestion and diarrhœa, have been recorded from its use. In the usual doses mental depression is seldom observed, but the drug should be used with caution in the emotionally unstable and in those who have passed through melancholic phases lest exacerbations recur Two 50 mg tablets of Raudixin, twice or thrice daily, the first dose on rising in the morning and the last twelve hours later, make a useful routine which may be supplemented by a phenobarbitone tablet, 30 to 60 mg at bed-time

If after a fair trial rauwolfia fails to maintain the diastolic pressure below 100, extracts of *Veratrum viride*, or hellebore, may be given in addition. Veriloid is a useful proprietary preparation of the active principles. It is available in tablets of 1 and 2 mg. Treatment may be started with 2 mg. four times a day, the dose being taken along with the quantity of Raudixin already prescribed. With this drug a maximum hypotensive effect is usually obtained with a daily quantity 2 to 4 mg. less than that required to induce toxic symptoms. The [illegible] oxicity is narrow, and may amount [illegible] period. Accordingly, the dose of [illegible] adding a 2 mg. tablet to the daily dose every third or fourth day until the earliest symptoms of intolerance develop. Heartburn, increased salivation, nausea or vomiting are the usual indications that the optimum daily dose has been exceeded. Veriloid intoxication subsides rapidly when the daily quantity is reduced by 2 to 4 mg.

Significant hypotensive effects can be induced in about half the patients taking this drug, more particularly if the maximum dose tolerated is taken steadily and in conjunction with Raudixin. Most patients feel better, are less

tired and are free from headaches when full doses of Veriloid are in use. Tolerance varies from patient to patient, and the daily effective quantity ranges

the patient to continue with it

Grade 3.—When signs of retinitis are present, or when the heart or kidneys are showing early signs of failure, more energetic measures are required, firstly for the relief of symptoms, which tend to be more severe in this group, and secondly in an attempt to arrest or reverse the obliterative vascular disease. In these circumstances treatment usually starts with a period of rest in bed for three or four weeks, during which insomnia is corrected and dietetic measures for weight reduction commenced.

Methonium Compounds.—In recent years new ganglionic blocking-agents,

its effects are longer in duration and it is about five times as strong. Its great advantage is that it can be given successfully by mouth to the majority of patients

The ideal method of adjusting pentolinium dosage to the patient's particular requirements is by measurement of the blood pressure, taken lying and standing, at frequent intervals through the day. This can best be done in hospital by trained technicians or nurses. Where such facilities are not available, a single reading of the blood pressure, taken in the erect posture and at a stated time of

intelligent and co-operative patient soon learns to regulate his pentolinium dosage. The dose varies from patient to patient: the only guide is the individual's response.

after breakfast, and records kept of the response from day to day until the dose is finally stabilised. If the patient is symptom-free in the erect posture after 20 mg. then the following day 40 mg. is taken at 8 a.m. and 8 p.m. In the absence of untoward reactions, the following day additional doses of 20 mg. each may be taken at noon and at 4 p.m. The aim should be to obtain an adequate

hypotensive effect from the morning and evening doses, with smaller doses in the middle of the day, at noon and 4 p.m. to extend the hypotensive effect throughout the day. Of the four doses the evening one can with advantage be the largest in the hope of prolonging the effect overnight, the midday doses the smallest, and the morning dose intermediate. After two or three weeks this exploratory approach to dosage (and the onset of tolerance in the patient) might—in an average case—result in a dose-schedule such as the following:

blood-pressure response to a test dose over a period of several hours. In these circumstances the aim is to reduce the systolic pressure to 120 to 140 mg. Hg.

Two difficulties in pentolinium treatment call for special comment. Tolerance to the drug develops rapidly at first and may in fact continue to develop to a slight extent for some months. The daily dose must therefore be raised day

bowel action is restored, thus resulting in severe hypotension. Pentolinium is less likely to cause constipation than other hexamethonium compounds, but nevertheless, the patient should be warned of its dangers and have a suitable remedy. A cascara pill or mixture may be necessary in generous doses. Parasympathetic stimulating drugs can also be used to combat the sluggish bowel and also the dryness of

carbachol, 0·25 mg.; or

used. If complaint is

strength of $\frac{1}{32}$ per cent. to $\frac{1}{8}$ per cent. may help, but sometimes it may be necessary to provide an extra pair of glasses, refraction being adjusted to the change in the eye brought about by the action of the methonium compound.

Indirectly, Raudixin has proved very effective in counteracting the side-effects of the methonium compounds When it is added to the methonium routine the response to pentolinium is enhanced, so that smaller doses prove equally effective. Side-effects of methonium are consequently diminished On account of its complete absorption from the gastro-intestinal tract and its protracted action, the powerful ganglion-blocking agent mecamylamine, has a more predictable and constant hypotensive effect than the oral methonium compounds. Its side-effects are similar and tolerance is readily established, so that dosage must be adjusted to the patient's particular requirements. It is wise to begin with a small dose, say 2 5 mg. at 7 a m. and 5 p.m As with pentolinium, the aim is to produce mild hypotensive symptoms in the erect posture two to three hours after taking the drug. Blood-pressure readings can usefully be made in the recumbent and erect postures about the same time. A substantial drop in systolic pressure to the region of 120 or 140, with a corresponding diastolic pressure of 70 or 80 in the erect posture, is desirable, provided hypotensive symptoms are not excessive. After two or three days, depending on the blood-pressure response, the doses of mecamylamine may be doubled, and

later, if necessary, additional doses may be added at 12 noon and 10 p m. To determine a steady therapeutic routine, a few weeks of careful study, during which the dose of the drug is "titrated" against the postural response, are usually required. It must be emphasized that the effective dose of all ganglion-blocking drugs can only be determined by trial and error and thereafter maintained by steady perseverance. Our experience with mecamylamine is so

daily quantity can often be reduced by the administration of alkalis.

Grade 4.—Patients in this category are gravely ill and commonly die within a few months in a confusional state, with or without evidence of left ventricular failure, and with varying degrees of renal inadequacy. Any success in treatment

retention Signs of uræmia are ominous. they herald the intractable stage of hypertension

If renal function is adequate, the blood non-protein nitrogen less than 50 mg. per cent, and congestive failure absent or controlled, the prospects of lowering pressure and of arresting the progress of the vascular disease are reasonably good. Oral mecamylamine is the drug of choice Raudixin should be administered at the same time. Recurrent bouts of vomiting may preclude the effective use of the oral preparations. Parenteral administration is then the only alternative The "retard" preparation of pentolinium can be used for this

supplementary oral dose of either pentolinium or mecamylamine may be given about midday and in some cases oral doses can later be substituted for the two injections As the patient improves, four oral doses of mecamylamine may conveniently replace the subcutaneous injections

If renal function is grossly impaired and the blood non-protein nitrogen in excess of 50 mg. per cent, the response to treatment becomes less and less satisfactory. Renal function may in fact further deteriorate with a reduction in

output is said to be increased With this treatment renal function sometimes improves in a remarkable way in these gravely ill people.

Apresoline has distinct limitations, as side-effects and toxic reactions are frequent. Headaches, flushings and palpitation are common Drowsiness, œdema of the skin of the hands and feet, and dryness of the mouth also occur, but fortunately tend to disappear after a few days when tolerance is gained. Side-effects which are more serious are conditions resembling rheumatoid arthritis and disseminated lupus, anæmia, hepatomegaly and splenomegaly may also occur.

When uræmia is established, drugs are of no avail, but in the earlier stages of renal impairment hydrallazine may prove remarkably effective. Over a period

of two or three weeks the blood pressure may fall significantly, renal function
at this stage that pentolinium
Profound falls of pressure may
when hydrallazine is also in
use. at first the dose should not exceed 20 mg. daily.

Contra-indications to Ganglion-blocking Compounds.—A word of caution is necessary regarding the use of ganglion-blocking compounds. Unless the doctor is prepared personally to supervise their use from day to day until the correct dosage is determined, and unless he succeeds in enlisting the intelligent co-operation of his patient, the indiscriminate use of methonium or mecamylamine

abandoned in favour of a stricter hospital routine.

Experience indicates that ganglion-blocking compounds are liable to aggravate uræmia. If renal function is seriously impaired, there is little or no hope of reversing the process. Degenerative changes in vital organs may be so advanced as to debar any hope of successful therapy.

These powerful drugs are dangerous in elderly people. They should not be used in the presence of advanced cerebral arteriosclerosis and it is probably wise to delay their use for two or three months after either a cerebral or a coronary thrombosis, lest an abrupt and profound fall in pressure predispose to further difficulties After a recent cerebral vascular episode, the combination of a low-sodium diet with rauwolfia, and later if necessary with Veriloid in addition, is

preparations are in use, but seldom gives rise to difficulty if the diet is suitably adjusted and mercurial diuretics used from time to time.

Other Procedures.—In the past a variety of procedures have been tried in the treatment of hypertension; some have been successful—even in the severest grades All methods of treatment have their limitations, but occasionally are warranted for one reason or another As time passes and as experience with the ganglion-blocking compounds increases, it is probable that these subsidiary methods of treatment will play a smaller part in the care of hypertensive patients.

Low Salt Diet.—For many years restriction of salt intake has been used in the treatment of the œdema of congestive heart failure and nephritis. A falling blood pressure usually accompanies a reduced intake of salt, but to be really effective not more than 250 mg. should be consumed daily.

RICE DIET

Breakfast—

½ cup of boiled rice (cooked in unsalted water), eaten with sugar or corn syrup or fruit juice if desired

One or more bananas.

Grapefruit juice, one cup, with sugar.

Mid-morning—

Lemonade (2 tablespoonfuls lemon juice with water and sugar).

Luncheon—

½ cup of boiled rice (cooked in unsalted water), eaten with sugar or corn s
or fruit juice if desired.

One orange.

Fruits—one cup of any of the following :

Apple (without skin)	Grapefruit	Plum
Apricot	Lemon	Prunes
Banana	Orange	Raspberries
Blackberries	Fresh peaches (without skin)	Strawberries
Cherries, sweet	Pineapple	Watermelon

Vegetables, cooked—one cup of any of the following :

Corn	Brussels sprouts	Cabbage
Dry beans	Squash	Cauliflower

Grapefruit juice, one cup, with sugar.

Mid-afternoon—

Orange juice, one cup

Dinner—

½ cup of boiled rice (cooked in unsalted water), eaten with sugar or corn syrup or fruit juice if desired.

Cooked vegetables, any of those listed above, ½ cup.

Fruits, any of those listed above, ½ cup.

Grapefruit juice, one cup, with sugar

One or more bananas

Evening—

One cup of pineapple juice

Vitamins and iron should be added to this diet.
Avoid dates, avocados, tomato juice or nuts.
No salt to be used in cooking or at the table

The Kempner rice-fruit diet provides 2,000 Cals. per day and contains 20 g protein, 5 g. fat, 200 mg. Cl and 160 mg. Na. A specimen diet suitable in the treatment of severe hypertension is presented above. The meals consist of rice boiled thoroughly for twenty minutes, served hot and somewhat dry, 240 g per day, in three courses with fresh or tinned fruits of nearly all kinds. Sugar is added as desired to augment the caloric value Barley-sugar sweets may be taken between meals. No meat, milk or salt is permitted for the first six weeks, by which time distinct improvement in the retinæ should be evident. At this stage one or two potatoes and a few ounces of meat may be added on one or two days each week, and later, if improvement is maintained, one-third of the fruit is replaced by vegetables and more meat is added It is claimed that two-thirds of those willing to co-operate receive great benefit, both subjectively and in the blood-pressure levels

Obviously, such strict dietetic treatment has its limitations A low salt diet s of danger to patients with the severer grades of renal impairment as it may recipitate uræmia. Few patients can tolerate such insipid food for more than few days However, if other forms of treatment have failed and if the patient threatened with blindness from gross retinitis and papillœdema, he will submit the hardship of an irksome diet for a little while

fifteen years. This operation includes resection of the splanchnic nerves, together with excision of the sympathetic trunks from the level of the ninth thoracic root to at least as low as the first lumbar. In expert hands it has yielded striking benefit in the severest grades of hypertension. In younger people, provided renal function is reasonably good and congestive failure has not occurred, sympathectomy may produce a regression of the papillœdema, a fall in pressure, a restoration of a sense of well-being, and prolongation of life. Results compare favourably with those of any other method of treatment at present available. It is, however, a major operation, occasionally followed by

response to surgery is most unlikely in the presence of impaired renal function; and patients who have suffered or are suffering from left ventricular failure do not tolerate sympathectomy—in contrast to methonium and mecamylamine therapy.

Bilateral Adrenalectomy.—From the observation that the low blood pressure of Addison's disease could be corrected, and indeed over-corrected, by the subcutaneous insertion of pellets of deoxycortone, the suggestion arose that bilateral adrenalectomy might be justified in the severest forms of hypertension Even with the help which cortisone and other substitution products provide, the

danger, suggest that there is little or no future for the employment of such a drastic procedure as adrenalectomy in the treatment of hypertension, except in the relatively rare case where the adrenal gland is primarily involved—as in phæochromocytoma.

Symptomatic Measures.—*Headaches.*—In most patients headache clears up within a day or two by the provision of adequate rest and sleep In resistant cases relief can sometimes by obtained by correcting the patient's sleeping . By keeping the head of the bed elevated at night on 6, 12 or 18 inch

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trinitrate in a dose of 0·2 mg ($\frac{1}{300}$ gr) up to 0·5 mg. ($\frac{1}{120}$ gr.) or more on waking in the morning. If this is unsuccessful, as it often is, then recourse must be had to the more purely symptomatic analgesics, and for this purpose a full dose of phenacetin, 0·3 to 1 g (5 to 15 gr), taken with a cup of hot tea on waking in the early morning, is generally very helpful. Tablets or powders containing aspirin, or calcium aspirin, with caffeine, and phenacetin, are often useful. It is remarkable how on occasion a patient may remain free of headaches for weeks on end after a profuse epistaxis or a generous venesection.

Vertigo and Tinnitus.—Sedatives are of most use. Chloral or barbiturates in small doses may be employed, but if ineffective after a short trial, a rest in bed

for a few days may be suggested. It has been shown that certain of the antihistamine drugs reduce the incidence of travel sickness commonly regarded as primarily a vestibular disturbance. This has led to their employment in the [illegible]

reduce their frequency.

The treatment of the actual attack aims at a lowering of intracranial tension and abolishing cerebral œdema. It is claimed that prompt relief, particularly in hypertensive fits, can be obtained by the slow intravenous injection of hexamethonium salts, 5 to 15 mg. The effects of the drug on blood pressure should be recorded, and subsequently control of the arterial pressure instituted.

Lumbar puncture is a risky procedure in these circumstances, the reduction in spinal pressure favouring impaction of the medulla in the foramen magnum. Soluble phenobarbitone, 0.2 g. (3 gr.) intramuscularly, can be used to arrest epileptiform attacks. McAlpine, having seen dramatic benefit result from the [illegible] commends its use in the treatment of [illegible] Similarly, the intravenous adminis- [illegible] or glucose (20 ml. of a 50 per cent. solution) or rectal [illegible]

a scalpel or a pair of scissors.

THE SENILE HEART

Past middle life the individual is more than ever at the mercy of his arteries; [illegible]

ment for these states will be found under the appropriate headings. In old age, with generalized arteriosclerosis, weakness of the skeletal muscles and diminution in the cardiac reserve advance step by step. For one reason or another old people tend to avoid exertion and may even deny themselves gentle exercise. They are therefore [illegible]

[illegible]

accomplished, and when signs of basal congestion become evident, digitalis is indicated, and may be given as digoxin, 0.25 mg. twice or three times a day for a

week or ten days at a time according to tolerance. If intermittent courses prove of value, then maintenance doses may be continued as necessary. When frank signs of congestive failure develop, special care must be taken in nursing with a view to the provision of the maximum amount of rest and comfort. The procedures outlined in the section dealing with the treatment of congestive heart failure are then applicable.

A. R. GILCHRIST.

THE CARDIAC ARRHYTHMIAS

The presence of a cardiac arrhythmia is an indication for treatment only when the abnormal rhythm interferes with the efficiency of the heart's action. Sinus arrhythmia is a normal mechanism and requires no treatment. Occasional extra-systoles, or even short bouts of paroxysmal tachycardia, may occur in healthy hearts with no effect on cardiac efficiency. Minor degrees of heart-block and auricular fibrillation with a slow ventricular rate are indications of [illegible]

this can be done without fundamental change in the abnormal rhythm.

AURICULAR FIBRILLATION

Treatment has here to be considered under two heads: (*a*) that of the disordered ventricular action resulting from the auricular disturbance; and (*b*) that of the disturbance of the auricular contractions, the fibrillation *per se*. Of these, the former is usually by far the more important, and as in most [illegible]

is worthy of consideration.

When auricular fibrillation supervenes in a person whose heart is otherwise relatively healthy (as in cases of toxic goitre, many rheumatic cases and cases of paroxysmal fibrillation), the ventricles beat irregularly at a high rate—over 120 and even as high as 180 per minute. The high rate, and the inefficiency conditioned by the total irregularity, usually determine the speedy onset of symptoms of congestive failure, and relief of these symptoms will follow reduction in [illegible] For this purpose preparations of the

[illegible] heart muscle is extensively fibrosed (old arteriosclerotic and hypertensive cases) frequently have slow, though irregular, ventricular rates in the presence of auricular fibrillation, since a damaged [illegible] a healthy bundle In such [illegible] pulse rate of 60 or 70 pe[illegible] are absent, and digitalis loses its dramatic effect.

[illegible]

cases by giving hypnotics, but there need be no hesitation in using morphine

This drug is relatively safe even in desperately ill patients, and often affords striking relief from sleeplessness due to dyspnœa. It is worthy of emphasis that the widespread mistrust of morphine in cardiac patients is baseless, and that the drug is of great value.

[illegible] should be fully digitalized without delay. The administration [illegible] e of preparation [illegible] ptoms and the [illegible] employed and whatever preparation is used, the patient should be kept under observation during the period of digitalization. The pulse rate is no real guide to the heart rate in view of the pulse deficit in such cases, and the apex-beat should be [illegible] during this period. In hospitals the senior nurses should chart

[illegible]

individual concerned. Patients who have been taking digitalis for months or years should be re-examined occasionally: instances are frequent in our experience where a patient has taken digitalis for long periods without adequate supervision, and where clinical examination reveals quite inadequate control of the heart rate, with consequent limitation of the exercise tolerance or even congestive failure Underdosage rather than overdosage is the rule in these neglected cases. Indeed it may be said in general that failures of digitalis in practice are frequent, and are almost always due to inadequate dosage The only method of assessing dosage correctly is by frequent examination of the patient

[illegible]

oxygenated and becomes less irritable; at this stage normal sinus rhythm is likely to supervene.

In cases with a low ventricular rate in the untreated state, digitalis is not indicated in the absence of congestive failure Should failure be present the drug should be given with due caution lest untoward bradycardia result. Some benefit results in many cases, but the results are less likely to be dramatic than in the usual cases with high ventricular rate.

[illegible]

hemiplegia in survivors are such that every measure must be taken to prevent such catastrophes. To this end long-term treatment with anticoagulants offers

some prospect of success: no absolute guarantee of immunity from emboli can be given, but the risks are greatly reduced (see p. 93)

Treatment of the auricular disorder may be considered when cardiac failure has been abolished. It is well recognized that a proportion of cases of auricular fibrillation can be restored to normal rhythm by quinine derivatives, particularly quinidine sulphate. The prospect of success and the duration of the restored normal rhythm in any given case vary with a number of factors, a full understanding of which is essential before the treatment is started as the use of the drug is not without risk.

The drug is of most value in cases of auricular fibrillation of comparatively recent onset, without grave signs of muscle damage (enlargement, etc.) and particularly when the exciting cause of the arrhythmia has been traced and

duration, or in patients with grossly enlarged hearts and congestive failure. Should normal rhythm be restored in such cases, it is likely to be of short duration, and the benefits obtained are not commensurate with the definite risk involved in the treatment. Cases, too, with a previous history of embolism are unsuitable for quinidine, embolism from an auricular clot being a known risk of quinidine therapy, and the risk being increased by similar embolic accidents in the past.

While from the foregoing it is evident that in our opinion quinidine is greatly limited in its value, it must in justice be admitted that in other centres the drug is much more freely used. It is argued that even a few additional weeks or months of normal rhythm is a considerable gain for a patient who is progressing toward the usual terminal phase of, say, mitral disease. On the other hand there are patients with mitral disease and auricular fibrillation whose dyspnœa is aggravated by the restoration of normal rhythm.

Should quinidine therapy be decided upon after due consideration, the drug should only be given after careful preliminary digitalis treatment. The ven- ... have been

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or even collapse. Should no toxic symptoms develop, the drug is given in doses of 0·3 g. (5 gr.) four-hourly throughout the twenty-four hours, with one dose omitted during the night to allow of eight hours' sleep; this dosage is kept up for several days or even a week. Electrocardiographic control is desirable, and careful clinical observation, preferably in hospital, essential. Should the fibrillation persist after this course, it is repeated after an interval of a week, during which digitalization is maintained. The proportion of cases that returns to normal rhythm varies with the type of case selected for treatment, but averages about one-third. In post-operative cases of thyrotoxicosis, practically all cases can be restored to normal rhythm—in fact, spontaneous reversion is common and may occur up to three weeks after thyroidectomy. The actual risk to life (from embolism, etc.) in well-selected cases seems to have been greatly exaggerated.

In our opinion quinidine is a drug requiring considerable judgment in selection of cases, and skilled observation and care during its administration.

It is a drug which has little place in general practice for the treatment of auricular fibrillation

AURICULAR FLUTTER

Unlike auricular fibrillation the disordered auricular mechanism in this condition is influenced considerably by digitalis In doses sufficient to produce ventricular slowing as in auricular fibrillation, this drug also causes conversion of auricular flutter to fibrillation in a considerable proportion of cases. The cessation of all digitalis medication in such a case, once fibrillation has developed, is followed in about one-third of the cases by return to normal rhythm; in another one-third the rhythm reverts to flutter, in the remaining one-third fibrillation persists as an established condition If flutter recurs, a second course of digitalis may succeed in establishing normal rhythm, or quinidine may be tried. If auricular fibrillation develops, it is treated in the usual way, and again quinidine may be tried In any case, the restoration of normal rhythm has the same prospects of duration as it has in cases of auricular fibrillation, and there is a similar risk of embolism

When digitalis is used, it is given in the same manner as for auricular fibrillation Careful observation of the patient (especially of his apex rate) is essential Whenever marked slowing occurs together with total irregularity at the apex, fibrillation may be assumed to have developed. This has occurred [illegible]

[illegible]

the rate of the auricular contractions, so that an auricular rate originally between 250 and 300 per minute falls gradually—it may be below 200 per minute. At this stage there is a danger that the ventricles may follow the full auricular rhythm (1 : 1 flutter) instead of responding to every second, third or fourth auricular cycle as at the beginning of treatment. Should this occur a dangerous tachycardia at 180 to 200 per minute may arise. This accident, however, is very rare The slowing of the auricular rhythm to 200 or thereabouts is frequently followed by abrupt resumption of normal rhythm. Large doses of the drug are then stopped, and after twenty-four hours small doses of 0 2 g. (3 gr) once or twice a day are given and maintained for a few weeks

It is our practice to use digitalis for cases of flutter in the first instance Quinidine is reserved for those which fail to respond to digitalis. In either case, should normal rhythm be restored, its duration depends on the same factors as apply in cases of fibrillation treated with quinidine. Recurrence of flutter or fibrillation at an early date is likely in cases with grossly enlarged hearts or old-standing disorders of rhythm, and in those where a toxic factor is still operative, such as hyperthyroidism

PAROXYSMAL TACHYCARDIA

[illegible]

In cases with an exciting cause, such as the last named, efforts should be made to remove it.

During attacks various measures may be employed to cut short a paroxysm. Any one of a number of procedures may result in the abrupt cessation of the attack, and many patients soon learn how to treat their own symptoms. The particular method which meets with success varies in individual cases, but frequently remains fairly constant for any particular patient. Bending the head low between the knees when seated on a chair, holding the breath, attempting forced inspiration or expiration with nose held and mouth closed, pressure over the abdomen, and vomiting, are all examples of procedures that patients may find useful in cutting short the attacks. The physician may stimulate the vagus

on a couch, and pressure with the finger-tips of one hand should be gently exerted over a point level with the upper border of the thyroid cartilage at the anterior border of the sterno-mastoid. During this time the heart should be auscultated, and abrupt slowing or cessation of the sounds is the signal for immediate release of pressure. In some instances a first attempt is ineffective, but success may follow repeated attempts or stimulation of the sinus on the other side. Cases resistant to such sinus stimulation may yield to reflex vagal stimulation through the fifth nerve, from pressure on the eyeballs. Ocular pressure, however, is unpleasant and painful, and is now seldom employed.

If all such attempts prove ineffectual, the induction of vomiting by emetics, or the production of nausea by subemetic doses of tincture of ipecacuanha, may cut short the attack. A tight abdominal binder is often effective, especially in children.

In cases in which these simple measures are ineffectual, attacks may sometimes be brought to an end by full digitalization, e g. by the intravenous injection of 1 mg. of digoxin. If this fails, quinidine sulphate by mouth in doses of 0.3 g. (5 gr.) three or four times a day may be effective. Hypodermic administration of 15 to 20 mg. ($\frac{1}{4}$ to $\frac{1}{3}$ gr.) morphine may secure needed rest for an anxious and exhausted patient.

With the development of symptoms and signs of congestive failure or of pain, indicating exhaustion of the heart muscle, the arrest of the paroxysm becomes more urgent.
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be achieved by the intravenous injection of a drug of the parasympathomimetic group, e.g. carbachol (B.P.). This is allied to acetylcholine, a sub-

readily in the body to be of value in therapeutics, but other more stable esters of choline share some of its properties. Of these, acetyl-β-methyl-choline (the chloride of which is marketed as Mecholin or Mecholyl) and carbaminoylcholine (which is also known as Doryl or carbachol, B.P.) may be given subcutaneously to refractory cases of paroxysmal tachycardia. Fraser advocated Mecholin as preferable for this purpose. A usual dose is 25 mg. intravenously, though as much as 60 mg. may be required. The effect is produced within a

minutes, and abrupt return to normal rhythm occurs in a high percentage of es. Carbachol is given in smaller doses (0·05 to 0·12 mg.), and is also effective. has been noted, however, to produce auricular fibrillation in some cases. With either of these drugs other symptoms of excessive vagal stimulation may occur—nausea, vomiting or diarrhœa

It should be remembered that the attacks tend to cease spontaneously and are generally of short duration—minutes or hours Every day that passes in a resistant case renders the spontaneous arrest *more* likely to occur within a short time, and whatever medicament is being used will probably be given the credit for the cure

Ventricular Paroxysmal Tachycardia is less common than the other form, and generally occurs in patients with grave myocardial disease, e.g. after recent coronary infarction, etc It may also occur from gross overdosage with digitalis. One rare form, however, is innocent and occurs in relation to exercise in apparently healthy people. In general, vagal stimulation is useless in treating these cases. Mecholyl, carbachol and allied drugs are of no value in this form of tachycardia and treatment by quinidine, procaine amide or digitalis is usually required Quinidine is given as for supraventricular cases, and is very effective the rate during the paroxysm may fall gradually under quinidine before normal rhythm is abruptly restored Digitalis, though it can produce paroxysms of ventricular *origin* as a toxic effect is, paradoxically, of value in arresting those of other origin. It is risky, however, in cases of recent coronary infarction, and in our experience inferior to quinidine Treatment in cases of ventricular tachycardia with grave cardiac disease and gross failure is a more urgent matter than in the average case of supraventricular origin, and in these cases a quinidine sulphate drip given intravenously is of great value. Quinidine sulphate in a concentration of 3 g. (45 gr.) *in* 500 ml. of saline is given by slow intravenous infusion at a rate of 600 ml (1 pint) in six to eight hours Such a drip may be kept up for several hours It is essential that a close watch be kept upon the heart rate, and if possible electrocardiographic control advisable Gradual slowing of the high ventricular rate occurs, with sudd reversion to normal rhythm in many cases after administration of *from* 0·3 1·5 g. (5 to 20 gr.) of the drug. Once normal rhythm has been restored, quinid sulphate by mouth should be continued as described below. The local an thetic procaine has an action comparable to quinidine in ventricular ect rhythms, and is commonly given continuously by intravenous drip in a d of 1 g per hour during operations on the heart Its cerebral excitant a precludes its use in the unanæsthetised patient, but its derivative, procain is happily devoid of this cerebral action, and can be used, for example, cardiac catheterization or for treatment of extrasystolic arrhythmias. It given orally in capsules of 250 mg., or intravenously. By this route 100 given at a time, and the injection repeated at intervals of a few minute total of 1 g The blood pressure should be repeatedly estimated d injection, since hypotension is a common side-effect. As with quin drug is unsuitable for use in general practice and is best reserved f use with electrocardiographic control where practicable.

Prevention of Attacks.—Patients who have recently had an attack mal tachycardia, or who are liable to repeated attacks, are general maintenance doses of 0·2 to 0·3 g. (3 to 5 gr.) several times daily period of weeks Any obvious exciting factor (exc

or alcohol; thyrotoxicosis; septic foci in teeth or tonsils, etc.) should be attended to. Many cases are resistant and attacks recur at intervals over long periods of years without serious effects on the general health.

HEART-BLOCK

The treatment of minor grades of heart-block is directed towards elimination of the cause. Little can be done by drugs to improve the conductivity of a damaged *a-v* bundle. Many cases are due to excessive dosage with digitalis, and clear up when the drug is withheld. Others are due to an intercurrent streptococcal throat infection, and subside as this clears up. Many occur in cases of active rheumatic carditis, and for these there is no specific treatment beyond the usual regime of rest and salicylate and possibly cortisone. A few cases are due to reflex inhibition of the bundle through vagal stimulation, and in these [illegible]

are very rare. In that very large group of cases which occur as part of an ischæmia of heart muscle brought about through arterial degeneration, we have no specific drug of any proved value, and iodide has not in our hands deserved its time-honoured reputation. It is to be realized that simple prolongation of the *a-v* conduction time, or the occurrence of "dropped beats", is of no moment as regards the mechanical efficiency of the heart. Long-standing cases of 2 : 1 heart-block may have little or no limitation of effort, and demand no special treatment It is to be emphasized, too, that digitalis is not advisable in cases of partial heart-block, as the drug may depress the bundle further and aggravate the condition.

Established complete heart-block is likewise not amenable to therapy. Such cases are usually due to scarring in the bundle region, which from the nature of things is irreparable. The management of such a case, however, is important: the patient should be warned to live within his reserve, and cautioned as to the risks involved by strenuous exertion, such as running upstairs, lifting heavy articles, etc. Unduly strenuous acts produce in such cases sudden syncopal attacks, since the heart is unable to accelerate to meet the demands for increased blood flow to the tissues, and the cerebral circulation suffers accordingly.

High-grade heart-block in an unstable state is manifested clinically in many cases by recurrent classical Stokes-Adams attacks, to relieve which therapy may be of some value. The treatment of such cases is dealt with under Cardiac Syncope on p. 559.

EXTRASYSTOLES

Extrasystoles occurring in young people with no other cardiovascular abnormality do not require treatment, and as a rule are very resistant to any medication. The patient should be reassured as to the innocent nature of his abnormality, should he be aware of it, and should not be allowed to permit the arrhythmia to interfere in any way with his normal activities. We are familiar with cases of persistent extrasystolic irregularity in healthy young athletes and in men who, having had the disorder for many years, have reached the allotted span without mishap.

Patients who are greatly troubled by abnormal sensations due to extrasystoles may require a sedative, such as 30 to 60 mg. (½ to 1 gr.) of pheno-

barbitone. There is some evidence that the barbiturates may also diminish the frequency of extrasystoles in some cases.

Extrasystoles developing *de novo* in a patient demand careful overhaul to exclude organic cardiac disease, and also a search for possible exciting factors, of which examples are: heavy meals before retiring to bed; flatulence; tobacco in excess; septic foci in teeth or elsewhere; and digitalis overdosage. During some hours or days following a myocardial infarction, extrasystoles may be conspicuous and should be regarded as potentially dangerous in such circumstances. Since they may herald a paroxysm of ventricular tachycardia or a fatal ventricular fibrillation their suppression is advisable using quinidine, 0·2 to 0·3 g. (3 to 5 gr.) twice daily or four-hourly as required; or procain amide, 250 mg four-hourly

[illegible]

digitalis to a patient already intoxicated by it is, of course, highly dangerous,

[illegible]

idine sulphate, given as above, is useful in some cases, and is relatively safer than digitalis in the first week after a coronary thrombosis

Coupled rhythm, or *pulsus bigeminus*, is usually due to overdosage with digitalis, and this explanation should be assumed correct until it has been disproved. Keeping this rule will avoid accidents from digitalis overdosage.

SINO-AURICULAR BLOCK, NODAL RHYTHM, ETC.

[illegible]

drug should be temporarily withheld.

SURGERY IN THE TREATMENT OF CARDIAC DISEASE

For certain cardiac conditions relief may be obtained by surgical intervention on structures not anatomically connected with the heart itself, as, for instance,

[illegible]

mitral stenosis, and the constricting bands were removed in some cases of chronic adhesive pericarditis. Then ligation of the patent ductus arteriosus and an operation for relief of coarctation of the aorta came into practice, and operations to improve the pulmonary circulation in cyanotic congenital heart disease and in congenital pulmonary stenosis were devised and practised by Blalock and

Taussig, Potts, Brock and others. Such operations now constitute a highly specialized branch of surgery. While operations for mitral stenosis and patent ductus arteriosus are within the compass of many surgeons, most intracardiac procedures imply teamwork on the part of cardiologist, cardiac surgeon and anæsthetist, while the rectification of complex malformations awaits the perfecting of highly specialized techniques (body cooling, assisted circulation, etc.) designed to secure a bloodless and quiescent heart for a few minutes at the climax of the operation. No attempt will be made here to enter into details of technique. It is enough to indicate which types of case may be submitted to operation, with the prospects of relief which may be attained.

Mitral Stenosis.—Operations for the relief of this lesion, originally introduced and abandoned many years ago, have now won a deserved and prominent place in the management of rheumatic valvular disease. Pre-operative assessment of the anatomical lesion and of other factors (age, rheumatic activity, heart size, myocardial function, disability, etc.) is essential if good results are to be obtained and a low mortality ensured. The overall mortality in skilled hands is about 4 per cent., including cases found to have gross calcification of valves or significant incompetence; in pure stenosis the mortality should not exceed 2 per cent. The ideal patient is a severely handicapped or disabled person, in whom mitral stenosis is an isolated lesion, the heart is not grossly enlarged, failure is absent or controlled, and in whom active rheumatic carditis has been excluded. Operations under the age of twenty are inadvisable (though sometimes imperative) on account of the risk of recurrence of stenosis through rheumatic relapse. At the other extreme of age, patients over fifty are probably past the optimum age for safety and maximum relief. Associated mitral incompetence, unless of trivial degree, contra-indicates operation, as do more minor grades of aortic valvular disease. Auricular fibrillation *per se* is no bar, but generally indicates heart-muscle damage and a rather impaired outlook.

One group of cases deserves special mention—the patients, often relatively young, in whom breathlessness on exertion is moderate only and disability slight

with extreme pulmonary congestion ...

threaten life, and may end fatally. *The victims should be dealt with surgically without delay.*

The feasibility of operative relief has modified greatly the outlook for the pregnant woman suffering from mitral stenosis. Mitral valvulotomy can be done safely well on in pregnancy (up to the seventh month) and is particularly valuable in patients who develop acute paroxysmal dyspnœa during its course.

Medical practitioners in many areas are reviewing all their cases of mitral stenosis with the above criteria in mind, and refer all likel[illegible] a cardiac unit for assessment and decision rega[illegible] operation.

Congenital Heart Disea[illegible] for the re[illegible]'s tetralogy, pulmonary stenosis, coarctati[illegible] and [illegible] us are discussed on pp. 577-580.

Pericardial Disease.—[illegible] on may [illegible] of purulent pericarditis, and the [illegible] of p[illegible] er or closed p[illegible] more or [illegible]

In cases of chronic constrictive pericarditis where the two layers of pericardium are matted together, possibly extensively calcified, operation is difficult and may be hazardous, but is rewarding. The amount of interference required will vary from case to case, but a very extensive " decortication " of the heart may be necessary, stripping from the surface of the muscle the mass of scar tissue and calcium which impede its movements. In many cases bands of scar tissue constrict the openings of the great veins, and these have to be divided. It is clear how great the technical difficulties may be, and in practice the surgeon must often rest content with partial operations. There is a tendency today to carry out operation early in the development of the condition before dense scar tissue and calcium plaques form

These operations on the pericardium offer such good prospects of relief with such a moderate mortality that all cases where constrictive pericardial disease has been diagnosed should be referred to a competent surgeon for advice

Operations for the Relief of Cardiac Pain.—The indication for surgical treatment in angina is pain, persistent over two or three months, of such severity

would hesitate to recommend for himself ".

The operative measures which have been used fall into three groups:

and physical stress of operation are avoided, while good results are claimed Thus in a collected series of nearly 1,100 cases in the U S A. in 1954 marked improvement occurred in 40 per cent , while a further 36 per cent yielded worthwhile results, and only 24 per cent were failures Radio-active iodine therapy is to be avoided during the reproductive years of life.

There remains for consideration the interruption of the pain pathways. The afferent fibres from the heart run in the sympathetic fibres and ganglia of the

yields good results. The injection is a relatively minor procedure, performed under local anæsthesia, and very effective when skilfully performed, though on occasion fatal syncope has occurred during the injection. In some cases an

Taussig, Potts, Brock and others. Such operations now constitute a highly specialized branch of surgery. While operations for mitral stenosis and patent ductus arter

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rheumatic relapse At the other

past the optimum age for safe

incompetence, unless of trivial degree, contra-indicates operation, as do more minor grades of aortic valvular disease. Auricular fibrillation *per se* is no bar, but *generally indicates heart-muscle damage and a rather impaired outlook.*

One group of cases deserves special mention—the patients, often relatively young, in whom breathlessness on exertion is moderate only and disability slight but who are subject to attacks of acute paroxysmal nocturnal dyspnœa Such attacks of cardiac asthma, exactly comparable to those of left ventricular failure in hypertension or aortic disease, occur in patients with mitral disease, associated with extreme pulmonary congestion from left auricular failure. These attacks threaten life, and may end fatally. The victims should be dealt with surgically without delay.

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discussed on pp. 577-580.

Pericardial Disease.—Surgical operation may be required in cases of purulent pericarditis, and the indications for establishing free drainage by open or closed methods are more or less as in cases of pleural empyemas (see under Pericarditis)

nerves has been shown to afford some relief. The operations in use, of which there are several, vary in the extent of sympathetic resection, up to the extensive two-stage bilateral lumbo-dorsal sympathectomy of Smithwick. Reports as to their efficacy are conflicting, but there is certain evidence that not only symptomatic relief but regression of retinal and electrocardiographic changes may follow operation. Similar improvement in some patients is produced by "bloodless sympathectomy", using the ganglion-blocking drugs (see p 589) Only in cases failing to respond should surgery be considered.

There is as yet no clear-cut body of opinion as to the indications for operations of this type By common consent patients over fifty years are generally excluded, as are those with symptoms or signs of advanced irreparable damage to brain, heart or kidney (cases of cerebral vascular disorders, angina, coronary thrombosis or renal failure) In the selection of patients the response of the blood pressure to sedation tests (sodium amytal narcosis) is commonly tested, but hard-and-fast rules are unwise in view of the largely unpredictable results of operation. There is general agreement that cases of malignant hypertension in younger adults (up to forty-five or so) should be considered in relation to surgery, since relief of headache and other symptoms is often striking and on occasion papillœdema and cardiovascular signs regress after operation Whether life is prolonged is debatable, but the patient may be spared intolerable distress. After operations of this type most patients develop a postural hypotension, which may prove troublesome for some time but is rarely a serious disability.

In summary, unilateral kidney disease is a rare cause of hypertension, but it should be sought for in all young hypertensives and in those with no family history of cardiovascular degenerative disease When found at any age, removal of such a cause frequently leads to lasting benefit. In the majority of hypertensives, the "essential" group of the age fifty and upwards, operation on the sympathetic nerves or ganglia is probably inadvisable In the younger age groups and particularly in the so-called malignant cases, sympathectomy should be considered, and the advice of a neurosurgeon sought after full clinical investigation of the case.

Thyroidectomy for Congestive Heart Failure.—This operation has been displaced by the use of radio-active iodine for ablation of the thyroid gland in patients in whom reduction of the B M.R to minimal levels is desired as part of the management of resistant chronic cardiac failure.

Subtotal Thyroidectomy in Cases of Thyrotoxicosis.—The subject is dealt with fully in the section on Diseases of the Thyroid Gland (see p 356), where the advantages and disadvantages of treatment by antithyroid drugs or operation are discussed Should operative treatment be considered necessary, it is sufficient here to emphasize two points First, that serious cardiac decompensation with auricular fibrillation is of itself no contra-indication to operation in cases of thyrotoxicosis Naturally, the cardiac failure should first be treated as a pre-operative measure, but the presence of severe cardiac decompensation, far from militating against operation, is an absolute indication that operation should be undertaken. No matter how late the case, how advanced the cardiac damage, there is no doubt that only harm can result from continued thyroid toxæmia. If the patient can be brought into a reasonable state, and the extreme congestion reduced, then operative removal of seven-eighths of the gland holds out a prospect of considerable amelioration, if not of cure, of the cardiac condition. Secondly, there is little doubt that many cases of thyrotoxic heart disease escape

of the possible pitfalls of the blind injection operations are avoided. In our experience a neuritis may follow the operation, but this has rarely been persistent or severe. It is most liable to occur where traction on the brachial plexus has occurred through difficulty in exposure of the ganglion, which is deep-seated and rather inaccessible. Horner's syndrome on the operated side is an inevitable sequel to the operation.

After such operations many [illegible]
restored to a fair degree of act[illegible]
Absolute relief from pain cann[illegible]
usually achieved. The objection raised by Mackenzie, that operation by relieving pain abolished the " red light " that signalled danger in over-exertion, appears to have been exaggerated. We have not met any instance where the abolition of pain has led to unfortunate results. The tenure of life in cases of coronary disease is notoriously uncertain, and an occasional unforeseen death in a case which has been operated upon should not too readily be attributed to the operation. We have noted further that many of the patients, though free from actual pain after operation, are still conscious of a vague sense of oppression on exertion, which indicates to them that the limit has been reached and acts as the warning against strenuous activity

In conclusion it must be emphasized that such measures are reserved for the exceptional case of angina. In particular they have no place in therapy until it has been established that the patient is not suffering from the acute type of angina which does undergo spontaneous remission after a few weeks of rest and medical treatment. The administration of radio-iodine is temptingly easy, but it must not be forgotten that success with the isotope spells permanent myxœdema—not an excessive price to pay for release from chronic intractable pain, [illegible]

[illegible]

mental animal, and that removal of the injured organ led to regression of the hypertension, opened a new line of approach to hypertension in man. There is ample evidence that in patients in whom unilateral kidney disease is accompanied by high blood pressure, removal of the functionless and ischæmic kidney is followed by striking and lasting clinical improvement. Such cases constitute only a small percentage of hypertensives, but in a recent review Platt advises that in the investigation of all younger patients with high blood pressure, say under the age of forty-five years, and in all of those with symptoms suggestive of renal (non-nephritic) disorder, an intravenous pyelogram should be made with later retrograde pyelography if necessary. Platt also believes that such urological investigations should be done in all patients with no family history of hypertension By such methods the relatively rare cases of hypertension due to unilateral kidney disease (hydronephrosis, calculus, pyelonephritis) may be detected and advantage taken of the striking benefits from nephrectomy. In a small proportion of cases of established hypertension the cause may lie in a functioning tumour of the adrenal medulla (phæchromocytoma) which is more typically associated of course, with paroxysmal hypertension. Such a cause should be sought for and excluded.

In the majority of patients no such lesion is present (essential and malignant hypertension). In these cases more or less extensive resection of the sympathetic

exercise up to the point of inducing a healthy degree of fatigue and restful sleep is by its invigorating character of value to the cardiac patient whose response to effort is not greatly impaired Moderation in food, in drink and in tobacco is to be encouraged.

The avoidance of infection, particularly infection of the respiratory tract, is of prime importance to the cardiac patient This is not always easy, but suitable clothing and an abundance of fresh air at all times, with adequate ventilation of the living-rooms at home and in the office and workship, decrease the risk. In the winter months particularly, when exposed to cold and damp, and when respiratory infections of minor degree are often rife, the cardiac patient is wise to avoid hot, stuffy rooms, crowded places of entertainment and public meetings. Infections of the nose and throat—catarrh and, in particular, bronchitis—throw a considerable burden on the heart and circulation, and may in themselves be responsible in susceptible subjects for a decline in the cardiac reserve and the actual precipitation of congestive heart failure It is therefore proper that when an infection becomes manifest, particular care should be taken, and the patient advised to keep to his bed until free of symptoms Otherwise the cardiac patient must be encouraged to take such exercise as he can up to the limit of his tolerance, provided always that he is ensured a sound and restful sleep each night. His activities are only to be restricted to such a degree that symptoms are avoided. He can take exercise short of producing dyspnœa or undue fatigue.

Exercise.—The amount of exercise suitable for the individual can only be found by actual experiment. Activities are only to be limited when they are sufficient to induce symptoms, undue fatigue, dyspnœa or pain Thus it is that the degree of circulatory impairment is gauged by a study of the patient's reactions to exer-

activity is requir

the more likely

indicate that his tolerance has been reached, and the rate and amount of work in the future must be reduced to conform with his endurance. Similarly, anginal pain is a symptom that requires intelligent interpretation by the patient. Physical exertion (among other things) makes additional demands on the heart—demands which can be met only in proportion to the patency of the coronary arteries Thus pain assumes a physiological significance. it is a signal that excessive demands are being made on depleted resources; it is not proof of an exacerbation of heart disease.

Simple restrictions designed to limit activity so that symptoms are kept in abeyance are all that is required in the first instance. Golf, tennis, riding, swimming and even hill walks are permissible, and should be encouraged. Improved tone of the skeletal muscles is associated with an increased capacity for cardiac work The activity permitted varies with each individual and with the

to cause fatigue, dyspnœa or discomfort. At this stage there is often slight œdema of the ankles towards evening. This is important: it indicates that more active measures are required if congestive failure is to be avoided. Social and

recognition. In cases of unexplained congestive failure in the middle-aged, especially with auricular fibrillation, and even in the absence of overt ocular or nervous signs of thyroid disease, the possibility of thyrotoxicosis as the cause of the myocardial failure should be kept in mind. Careful search for signs of hyperthyroidism such as loss of weight, sweating, glycosuria, etc., and a full examination of the thyroid gland may reveal the true cause of the heart symptoms. Again, hypertension and hyperthyroidism frequently coexist, and relief from one burden at least can be secured for the heart by judicious treatment. Paroxysmal auricular fibrillation in apparently healthy people should likewise suggest careful examination to rule out hyperthyroidism.

I. G. W. Hill.

THE MANAGEMENT OF THE AMBULANT CARDIAC PATIENT

The energetic treatment of heart disease is chiefly concerned with measures to counteract the more advanced grades of the different types of heart failure, but it is no less important to learn the management of the minor degrees of incapacity in order that life may be rendered more tolerable, and serious failure avoided or postponed. The great majority of cardiac patients are able to go about, and, though their activities are restricted, yet with suitable guidance from time to time they can generally lead useful, moderately active lives. Their [illegible]

[illegible] occupation, the environment, the economic circumstances, the habits and, not least, the man's character and outlook influence treatment in its widest sense.

Briefly stated, the objects in treatment during the ambulant stage are to arrest or retard the downward course by decreasing the cardiac burden and also to improve the general health of the patient so that the liability to infection is [illegible] r living [illegible] ent his habits of life, so that these may be adjusted to conform with physiological principles. Hours of work and hours of sleep are a first consideration. The [illegible] 'nd or another [illegible] night, and for [illegible] Nine to ten [illegible] t be spent in actual sleep, the mere rest and relaxation is of very definite value, particularly if it become a regular habit

Hours of work vary enormously in different trades and occupations. Certainly in the minor degrees of cardiac embarrassment a maximum of eight hours is as much as most people can accomplish ; if more is attempted, then suitable intervals of rest should be provided. Each individual requires special consideration, but there is no doubt that the avoidance of the rush and tumble of everyday life, and the substitution of regular habits and a quiet and moderate routine, with gentle outdoor exercise from day to day, promotes general well-being. On the other hand harm results from too sheltered a life Muscular

already been pointed out that every attempt should be made to educate the rheumatic child so that in later life he may earn his living in a sedentary occupation.

In caring for these children the doctor should be prepared to advise the parents regarding the child's employment. In this country an outdoor occupation is inadvisable. Work involving physical strain and sudden or sustained muscular effort is likely to prove detrimental Employment at a bench, desk or counter is usually preferable. Clerks, book-keepers, typists, telephone operators, cashiers, dressmakers, tailors, all hold sedentary jobs suitable for the young cardiac patient. Similarly, there are such skilled trades as electrical mechanics, radio-repairers, watch, fountain-pen and jewellery makers to which the youthful [illegible]

[illegible] responsibilities and ease the burden It depends on circumstances whether restriction should be applied first to the daily occupation or to the hobbies and philanthropic activities. Too many men retire from active work without sufficient interests to occupy their minds The business man in early middle life, handicapped by organic heart disease, must of necessity be advised to limit his ambitions, lead the quieter life, have longer holidays and rely more and more on his staff for all routine work A day in bed once a week allows recuperation for the cardiac patient, and the results are often most gratifying

THE CARDIAC NEUROSES

The conception of the heart as the organ of emotion dates from the earliest [illegible] circulation, notions which contain more than a nucleus of truth It is a common- [illegible] and ideas—even those of a trifling nature These reactions may well be intensified a hundredfold in the face of major emotional experiences Sudden grief, joy, anger, shame, fear and such-like may each impose stress on the circulatory system, with the production of acute symptoms ranging from a mere blush to severe palpitation, giddiness, syncope, precordial discomfort, profound collapse or even sudden death [illegible] somatic and psychological

A week or ten days in bed will often enable the circulatory incapacity to right itself, and thereafter, when gentle activity is resumed, it will usually be necessary to insist on at least one day in bed each week, a rest of an hour or two after the midday meal, and the regular addition of an extra hour in bed each night for some months. Digitalis may be given in small doses of 60 to 120 mg. (1 to 2 gr.) of the powdered leaf thrice daily, generally for a week or ten days at a time with three or four days of freedom from the drug.

Focal Sepsis.—Foci of sepsis must be eradicated. Particular attention should be paid to the nose and throat. Regular dental inspections and treatment are, of course, indispensable. These measures reduce the risk of toxæmia and the hazard of respiratory tract infections. Dental and other operations call for penicillin "cover".

Anæmia.—Anæmia may materially aggravate the symptoms of cardiac insufficiency. Blood examination is part of the routine investigation: if anæmia is discovered it should be carefully assessed and the appropriate treatment given (see p. 399).

Such minor measures as these will do much to maintain the cardiac patient's general health and improve his response to effort, but if with the passage of time a further stage of decompensation is reached, and the tendency to congestive failure, nocturnal dyspnœa or anginal discomfort increases, then longer periods of rest are obviously required. The active therapeutic measures for these different types of heart failure are fully discussed on p. 519 *et seq.* In convalescence, after failure has been adequately corrected, drug treatment is almost invariably [illegible] from week to week. Digitalis in [illegible]

[illegible]

determining suitable treatment In infancy, for instance, the severer grades of congenital heart disease necessitate advice regarding feeding and nursing (p 236). The rheumatic child, when the active infection has subsided, requires much the same after-care as the tuberculous patient. Thus, prolonged semi-convalescent treatment in an institution has much to recommend it, for here the child's education may be continued without the rough and tumble of school life. In this country various residential homes are available where, under prolonged supervision, with adequate control of the diet, rest, exercise and lessons, better progress can be made than in the environment in which the rheumatic infection was originally acquired. Treatment at this stage is directed more to the prevention of infection or its reactivation than to the actual cardiac disease. It has been known for many years that streptococcal infections about the throat, nose and pharynx are particularly prone to reactivate the rheumatic process and thereby lead to further damage in the muscle and valves of the heart. Sulphonamides and penicillin have their prophylactic uses in the subjects of rheumatic heart disease. In the autumn, winter and spring months, when upper respiratory tract infections are rife, a measure of protection can be afforded by 0 5 to 1 0 g. [illegible] ml. (600,000 [illegible] When the [illegible] esume even modified school life, after care is req [illegible] s prevented, excessive fatigue avoided and exposure to cold and damp minimized, all of which are known to lower resistance and favour reactivation of the carditis. It has

it is his diagnosis that is "strained". These are terms to avoid. It is always a mistake to offer a half-hearted diagnosis; and adverse comments about the integrity of the heart are never justified without painstaking study of the history and a complete clinical examination. Only then is it possible to assess the relevant facts. Such a diagnosis as a "weak" or "tired" heart may sow the seed of a protracted cardiac neurosis on very fertile ground. A hasty remark, a look or a nod, even an expression of doubt on the face of the examiner, may rouse fears of crippling disability The vital function of the heart is known to all, and therefore symptoms are easily magnified, unless checked decisively at the earliest opportunity. Later, doubts accumulate and become more and more difficult to dispel.

Faced with such a problem, the doctor's first step is to take a detailed history and make an exhaustive physical examination. This is indispensable as a matter of routine and, in the special circumstances, to gain the patient's confidence. The electrocardiograph and the X-ray have their therapeutic as well as their diagnostic uses The examiner being satisfied in his own mind as to the nature of the disturbance, he must further strengthen the patient's confidence

professional competence; the patient must *there and then* be converted absolutely to the belief that he has a normal heart, the "atmosphere" of this consultation cannot be recaptured "when he has more time", it is a case of "now or never". Further, the physician must have the courage of his convictions. he has diagnosed "no evidence of disease", it is therefore a contradiction in terms to prohibit sport or to prescribe cardiac tonics.

ANXIETY STATES

It may well be that the basis of the cardiac neurosis is more deep-seated and repressed, so that only the special measures of the trained psychiatrist are likely to be fruitful The family doctor, who is prepared to devote time and care to his patient, and has the opportunity to study him as an individual, knowing his upbringing, his personal traits and frailties, can do much to help and guide the neurotic. An earnest endeavour to analyse the particular situation and define the source, origin and nature of the conflicts by frank discussion will accomplish far more in the long run than is to be attained by either hasty and injudicious instructions to take a rest at a spa or a sea voyage in the tropics. Repeated prescriptions for bromide, phenobarbitone or other sedatives accomplish little. The congestion of neurotics at health resorts often accentuates the patient's difficulties and widens the scope of his symptoms

Genuine emotional disturbances, reflected in circulatory symptoms, may result from all kinds of stresses and strains in modern civilization. Domestic

their real significance is appreciated, confidence gained and the facts faced in their true perspective, the patient comes to appreciate that his difficulties are often

In this normal reaction of the heart and circulation to emotional stimuli we have the basis of an understanding of the altered mechanism of the cardio-vascular system in those varied conditions which are roughly classified for descriptive purposes as functional circulatory states. Imaginary heart disease, neurocirculatory asthenia (the effort syndrome), angina innocens and the cardiac neuroses form a group of different but related conditions associated with much distress, disability and economic incapacity. Often they are entities in themselves unrelated to any structural defect in the heart or circulation. This is not the place to review in detail the symptomatology of these various functional states, but as a general rule they are the products of conscious or unconscious emotional trends—nearly always regarding current affairs and anxiety for the future. It is equally true that a patient may constantly complain of disagreeable sensations identical with those produced by a passing emotion in a healthy individual without being aware at the moment of any exciting cause. In other words, an emotion can act without being correlated in consciousness, and from the point of view of treatment such disabilities are less easy to detect and eradicate The psychiatrist may divide such patients into groups designated anxiety states, obsessional neuroses and conversion hysterias. Again there may be a true psychosis—sometimes associated with cerebral arteriosclerosis or hypertension.

It is important to realize that not infrequently a functional nervous state consorts with an organic lesion, and treatment is therefore all the more complex. True angina pectoris is an outstanding example of an organic disease in which violent attacks may be induced by transient emotional disturbances recognized by the patient as anger, fear or worry.

Similarly in rheumatic heart disease, long-continued anxiety with doubts and fears for the future may be the means of inducing a succession of symptoms mimicking serious disease. This is not uncommon in mitral stenosis—symptoms being partly organic, such as dyspnœa and fatigue, and partly functional as sub-mammary pain and giddiness *The knowledge, or even the suspicion, that the heart is the site of a morbid process is sufficient in the mind of many people to induce a train of symptoms based on fear, and ending ultimately in a deep-seated anxiety neurosis if unchecked at their beginnings*

The emotional reaction to doubt is apparently more intense in the case of the heart than of any other organ of the body. In the mind of the layman cardiac disabilities spell incurable disease and the oppressive expectation of sudden death. Only in the last stages of heart disease can it be said that there is a decreased response to emotion It is remarkable that so often individuals in the final stages of congestive heart failure are naturally sanguine and retain, despite all their discomforts, an optimistic outlook. They are brave patients.

IMAGINARY HEART DISEASE

The term imagined heart disease is best applied to those conditions which give rise to signs or symptoms simulating those of true organic disease, but in which the heart is not the seat of any structural defect. Innocent murmurs, precordial aches and simple syncopal attacks often suggest organic disease to the mind of the individual, a doubt which is intensified by an inadequate diagnosis and a faulty explanation of the mechanism of the production of the symptoms. It has been well said that the diagnosis of a " weak heart " or a " strained heart " h circumstances is a reflection on the doctor: it is he who is " weak ";

it is his diagnosis that is " strained ". These are terms to avoid. It is always a mistake to offer a half-hearted diagnosis; and adverse comments about the integrity of the heart are never justified without painstaking study of the history and a complete clinical examination. Only then is it possible to assess the relevant facts. Such a diagnosis as a " weak " or " tired " heart may sow the seed of a protracted cardiac neurosis on very fertile ground. A hasty remark, a [illegible]

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patient. Nevertheless, in the life of the patient this is a great occasion, and the doctor must never forget it: success hinges on the capacity of the doctor to dominate the situation, and he must do so with the fervour which derives from professional competence; the patient must *there and then* be converted absolutely to the belief that he has a normal heart; the " atmosphere " of this consultation cannot be recaptured " when he has more time "; it is a case of " now or never ". Further, the physician must have the courage of his convictions; he has diagnosed " no evidence of disease ", it is therefore a contradiction in terms to prohibit sport or to prescribe cardiac tonics.

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their real significance is appreciated, confidence gained and the facts faced in their true perspective, the patient comes to appreciate that his difficulties are often

less embarrassing than might at first sight be imagined. In this way the family doctor can often lighten the burden and reduce emotional tension. Circulatory symptoms can thus be eased and in time they may vanish completely. Simple explanations of the effects of pent-up emotions on the heart and circulation gradually come to be understood as confidence is regained. Drugs are usually not required. Insomnia must be corrected as adequate sleep is a first essential. Repeated examination of the heart and daily or weekly records of blood pressure are to be avoided, as thereby *attention continues to be fixed on the circulation.*

Recovery is slow; relapses are not uncommon; treatment or supervision is necessarily protracted Ross has shown that a large number of patients affected by the common neuroses, who are treated by a frank discussion of their symptoms, *will become well and keep well. By demonstrating how symptoms* arise as emotional reactions, by proving how they are retained because they are misinterpreted and by persuading the patient to appreciate their real value, much can be done to restore him to everyday activities. It is, in short, a method *of restoration of confidence combined with the banishment of fear* (Ross). Anxiety produces mental and physical exhaustion, and when this is adequately corrected by a short rest and by ensuring regular sleep, it is right that these people should be encouraged to take exercise freely.

Constant encouragement, persuasion and a judicious optimism can rescue many from lives of incapacity. It is useless to offer to the confirmed neurotic the bald statement, even after a thorough examination, " Your heart is sound: go away and forget about it." An encouraging clap on the back serves only to increase his discomfort. To him his symptoms are genuine and he has had no explanation for them. He now distrusts the doctor and the neurosis is accentuated.

THE EFFORT SYNDROME

The effort syndrome or neurocirculatory asthenia is worthy of more detailed study in view of its intractable nature. Here, as in the simpler neuroses, it is our first endeavour to offer an explanation for the symptoms, reassuring as far as is justifiable and explaining the nature of the nervous and circulatory upset. The eradication of sepsis is important, but the most successful measures are those directed to simple outdoor exercise governed again by the patient's endurance, so that confidence is regained The neurasthenic must be made to do more than he thinks he can. *Light walks, gradually increasing in range and in rate* for half an hour or so morning and afternoon, are of great benefit, associated later with a gentle outdoor occupation. These patients must be well fed and have ample hours of sleep. Drugs are of little or no value, and digitalis, as in all the neuroses, should not be prescribed, as by increasing the force of contractility it is liable to make the patient more aware of his heart. In any case, it does nothing to improve the circulation in health. The occurrence of this syndrome in the convalescent period after such acute illnesses as influenza, pneumonia or even tonsillitis, *particularly in young adults*, calls for special care in selecting an appropriate time for return to work. A hasty convalescence predisposes to this form of functional cardiac instability. Rehabilitation should include a spell of fairly vigorous exercise—a ten-mile walk or eighteen holes on the golf course—*and the significance* of this performance should be underlined by the doctor.

Treatment is rendered more complex when functional states and organic

disease coexist It requires a fine discrimination to steer a middle course, combining reassurance and encouragement with such physical limitations and drugs as the heart itself demands. In particular, in coronary disease associated with angina, and hypertension, there is almost invariably an undercurrent of emotional tension. This must be corrected by a frank discussion regarding simple rules of behaviour, and by the demonstration that fear is often unfounded. For this reason it is usually as unwise as it is unkind to say to a patient: "You suffer from angina, but the prognosis may run to ten or twenty years." Such a statement [illegible] ation of his [illegible]

A. R. GILCHRIST.

DISEASES OF THE BLOOD VESSELS OF THE LIMBS AND THE EFFECTS OF COLD

NORMAL PERIPHERAL BLOOD FLOW

THE *AMOUNT* of blood which reaches the tissues of the limbs depends on the calibre of the arterial tree, which in turn depends on the tonus of the smooth musculature of the arteries. Arterial tonus is controlled (1) partly by the activity of vasoconstrictor fibres belonging to the sympathetic nervous system, which are ultimately distributed to the vessels by way of the somatic nerves of the limbs, and (2) partly by the influence of chemical substances, either manufactured locally (products of muscular activity, which cause *vasodilatation*) or conveyed by the blood stream (adrenaline, which causes vasoconstriction). The arterial vessels may be grouped in two sets: those supplying the muscles, which are controlled mainly by the mediation of chemical substances, and those supplying the skin and subcutaneous tissues, in the control of which the sympathetic nervous system plays much the more important part. The latter set of vessels takes part in the general vascular reactions which help to maintain the body at a constant temperature. When the temperature of the environment changes, that of the blood tends to follow the changes. The [illegible] the temperature of the

[illegible]

with a correspondingly [illegible] generalized vasoconstriction of the superficial vessels is the response, which results in conservation of bodily heat. Adaptation to low environmental [illegible] hands and feet which [illegible] ilation [illegible] ineous arterioles and veins. When these anastomoses are relaxed by their controlling nervous mechanism, the resulting rapid increase in blood flow quickly warms the extremities.

For the development by the tissues of an adequate response to trauma and to bacterial infection, it is essential that both the peripheral vessels and the mechanisms for controlling the flow of blood in them should be normal.

PATHOLOGICAL PROCESSES WHICH REDUCE BLOOD FLOW

The processes which reduce the amount of blood flowing through arterial vessels may be classified into two groups:—

GROUP I.—AN ORGANIC CHANGE IS PRESENT FROM THE FIRST IN THE LUMEN OR WALL OF THE AFFECTED VESSELS

A. Thickening of the wall of arteries: In arteriosclerosis, syphilis and juvenile arteritis.

B Embolism: The embolus may (1) originate in the heart (auricular fibrillation, infarction, bacterial endocarditis), (2) be detached from an atheromatous patch in an artery, or (3) break away from a venous thrombus, and reach the arterial tree by way of an atrial septal defect.

C. Thrombosis: (1) In arteriosclerosis (elderly patients of both sexes, especially diabetics); (2) in thromboangiitis obliterans (young or middle-aged ... and leukæmia; ... ter debilitating

Group II.—The Obstruction to Blood Flow is offered by Spasm of the Vessel, and Organic Changes are (at least at first) Absent.

A As a result of trauma: In arteries of medium size, particularly after bullet wounds in their vicinity

B. As a result of local hypersensitivity to cold: This is encountered in the

...

spasm These tend to increase and to perpetuate the obstruction to blood flow.

SUDDEN OBSTRUCTION OF LARGER ARTERIES

When a main artery is obstructed by an embolus, the patient experiences numbness or pain in the limb and the skin becomes at first blanched and later cyanosed. Pulsation is absent beyond the site of lodgment of the clot. The temperature of the skin falls slowly to that of the environment. Loss of sensation and of power appear, and progresses from the distal parts towards the proximal Muscle contracture follows within a few hours. The area involved in these changes depends on the availability of collateral vessels If they are inadequate, whether anatomically from reflex vasoconstriction or because consecutive thrombosis leads to obstruction of their origins, a sharp line of ... Distal

... l to the prevention of consecutive thrombosis by the administration of heparin (see ...

Embolectomy is required as the primary treatment when the clot obstructs (1) the aortic bifurcation, (2) a common iliac artery, (3) the bifurcation of a common femoral artery, and (4) the third part of an axillary artery.

GRADUAL OBSTRUCTION OF ARTERIES

In practice this is a very common condition. As a rule, the morbid process affects both the superficial vessels and those of the muscles; but not infrequently the clinical features may direct attention particularly to one set, and they will be described from this aspect.

The Superficial Vessels

Cold Feet.—When the patient complains of cold feet this is usually accompanied by changes in colour. Cyanosis is often present, and always indicates a slow circulation; if present in warm surroundings, it must be regarded as abnormal. If the temperature of the environment is constant and the surface of the skin dry, the temperature of the skin provides an index of the efficiency of the superficial circulation. For accurate observations, thermo-electric skin-thermometers are necessary ; in clinical [illegible]
estimation may be m
the dorsal surface of
where the circulation

Nutritional Changes.—The growth of the nails may be greatly retarded, and perspiration diminished or absent. Any breach of the epithelium heals very slowly or not at all, and indolent ulcers may appear on the heel and in the interdigital clefts of the toes. As the vascular occlusion progresses, areas of digital dry gangrene may develop, and this is often precipitated by careless nail-cutting or corn-paring (p. 619) In the final stages the foot, or the foot and leg, may become gangrenous. Both ulcerative and gangrenous processes are, as a rule, extremely painful.

The Deep and Superficial Vessels

The patient may complain of pain. The cardinal symptom of inadequate blood flow to the muscles is intermittent claudication, a cramp-like pain usually in the calves which restricts exercise. This appears most rapidly if the patient walks uphill or fast, and in its most severe form it may force him to halt after he has walked as little as fifty yards. Claudication disappears if the patient rests.

Very inadequate blood flow in both superficial and muscular vessels is sometimes associated with severe pain which occurs during rest, especially at night; this is usually felt in the heel and/or in the sole of the foot.

In every case in which the history or physical signs are suggestive of arterial insufficiency, the pulses of the limbs must be carefully examined; this should be done when the subject is warm, because pulsations are then maximal. This examination does not supply complete proof of absence of blood flow, because (1) vessels may pursue an abnormal course, (2) additional abnormal vessels may be present, (3) a partial obstruction proximally situated may diminish pulsation without seriously reducing blood flow (e.g coarctation of the aorta), and (4) although the walls of a [illegible]
a fair quantity of blood.
of adjacent tendons for
posterior tibial arteries.

General Treatment.—The heavier the patient the greater the strain on his feet and legs; therefore any tendency to obesity must be corrected (see Treatment of Obesity, p. 324). If diabetes is found to be present it must be meticulously controlled because it may be of ætiological importance and because it predisposes to septic complications. Otherwise, since no individual food factor is known to be of ætiological significance there is no indication for interference with the patient's dietetic habits. Alcoholic beverages, in strict moderation, are harmless and, indeed, whisky at bedtime may, in virtue of its action as a mild vasodilator, be beneficial in such cases. Cigarette smoking must

be stopped completely. Rest pain is usually relieved by placing the legs in a dependent position, and the patient may be able to sleep in a chair or with the head of the bed raised, but prolonged dependence must be avoided because the resulting œdema further embarrasses the local circulation. It is a wise plan to arrange for the patient to have a succession of good nights at the beginning of treatment, by giving a mild hypnotic-analgesic such as butobarbitone, 0·2 g. [illegible] acetylsalicylic acid, 0·3 g. (5 gr.). Lack of sleep makes these old [illegible] after a good [illegible] old with him. [illegible] clothes should

[illegible]

[illegible] feet and legs must be washed daily [illegible] dried with a [illegible] ould be woollen, seamless and of a goo[illegible] ots and shoes must be roomy without being loose, without irregularities (nails) which might press on the soles of the feet, and should have a rubber sole over the leather one. Prolonged standing is harmful. The feet must be protected from even the slightest trauma; thus toe nails should be cut straight and well away [illegible] and never treated with [illegible] services [illegible]'s doctor [illegible] ist avoid [illegible] ts. And finally, the feet and legs must never be exposed [illegible] old water.

Care of Nutritional Lesions.—The appearance of any breach of surface, however trifling, is of such potentially grave moment that the patient must rest [illegible] be gently cleansed with [illegible] position [illegible] circle a [illegible] s a rule [illegible] plication [illegible] of saline

[illegible]

order to promote drying. Mechanical attempts [illegible] slough should seldom be made. The local application of heat is not good [illegible] increases the demand on an [illegible] hould never be [illegible] en the decision [illegible] osclerosis local removal may be considered if the tissues appear [illegible] g well on the

[1] Cinchocaine (B.P.); Lignocaine (B.P.)

proximal side of the gangrenous toe; the incision should follow the line of demarcation, and the skin proximal to this must not be handled with forceps. The wound should be left open, or at most one loose stitch inserted. Local anæsthesia must not be employed to remove gangrenous digits, because it [illegible]

an angry reddening of the skin is seen about the base of a gangrenous digit, perhaps associated with lymphangitis of the foot and leg. This often heralds extension of the gangrenous process, but occasionally it is due to retention of pus by the hard skin of the gangrenous area; before more extensive measures are tried, *search should be made, particularly in the sole and interdigital clefts,* and any small abscess drained by raising the dry black skin.

It must be emphasized again that if a small gangrenous area such as a digit is left to separate spontaneously, which is often the wisest plan, pain must be *controlled especially at night; but only as a last resort should morphine or one* of its derivatives be employed for this purpose.

A major amputation is required (1) when gangrene is massive from the first, (2) when gangrene involves more than digits and (3) when ischæmia gives rise to intolerable pain. The relatives should understand that the pathological process is bilateral and that the other leg may be affected at a later date.

Measures Designed to Improve Blood Supply.—1. *Drugs.*—Numerous attempts have been made to improve blood flow by the administration of drugs. Their use alone is not recommended.

2. *Operation.*—An attempt may be made to improve the total blood flow in the limb by sympathectomy. The result of such an attempt depends on the availability of collateral channels, and/or their capacity to dilate. This can be determined by tests, which must be carried out in a hospital properly equipped to do so. Sympathectomy is indicated only in early cases of arteriosclerosis; in thromboangiitis obliterans, operation should not be undertaken except after very careful preliminary study It must be emphasized that *claudication is rarely benefited* by sympathectomy, because the control of muscle vessels is predominantly chemical.

[illegible] involves only a short segment of a major artery, some [illegible] the obstructed segment by [illegible] e process is nearly always *generalized and progressive,* so that cases suitable for grafting are few and the ultimate value of this procedure remains to be determined.

Measures Designed to Prevent Thrombosis.—The introduction of the indanedione group of anticoagulant drugs has made safe and economic the prolonged administration of anti-coagulants. The value of this measure in peripheral vascular disease has not yet been fully assessed and at present its use should be restricted to patients with severe or rapidly extending disease.

INTERMITTENT OBSTRUCTION OF ARTERIAL VESSELS

This group includes the cases in which the Raynaud phenomenon *is the* presenting physical finding. The essential feature of the commonest type which is met with in young women consists of attacks characterized by the sudden arrest of the inflow to the fingers, and possibly to a less extent to the toes

Usually an attack is precipitated by exposure to cold. At first nutritional changes are absent, but in severe cases of long standing, areas of superficial [illegible]

[illegible] make this difficult, at the least the patient must avoid cold in its most provocative form—cold water. Much can be done to reduce the frequency and severity of attacks by the adoption of proper clothing The trunk should be warmly clad in order to minimize the amount of vasoconstrictor tonus imposed on the peripheral vessels The limbs should be warmly clad from the root of the limb (clavicle, groin) to the hands and ankles; this keeps the blood warm on its way to the digits For the hands, warm, loose-fitting gauntlet gloves are essential; for the feet, stout boots or shoes, allowing room for two pairs of stockings, and with additional rubber soles. The patient should sleep in a warm bed between flannelette sheets or blankets, with arms and hands under the bedclothes, so as to ensure at least eight hours each day of inhibition of vasoconstrictor tonus

When the condition follows the use of vibrating tools, the workman must find other employment

[illegible]

is often sufficien[illegible]

Operative [illegible] best possible conditions, and the attacks continue to be a source of economic or social disability, operation may be considered This takes the form of division of the sympathetic vasoconstrictor fibres to the limb, and, if the point of section is properly chosen, worth-while vasodilatation of the superficial vessels follows Of necessity, sweating is also abolished and the dryness which results may be troublesome in the hands [1]

Sympathectomy operations are not dangerous, and the period of disability is short (two or three weeks). No serious undesirable after-effects follow a well-planned operation.

Erythro-cyanosis

This is the term employed to describe a condition which occurs almost exclusively in adolescent and young adult females. It is characterized by areas of defective circulation situated on the legs, particularly on the antero lateral aspect, just above the external malleolus Such areas are bluish-red in colour, and the skin is atrophic. The patients suffer in addition from cold feet, and burning pain is commonly felt when the blue areas are warmed The condition is, as a rule, present only during cold weather In advanced cases ischæmic necrosis of the subcutaneous fat may occur and the skin may actually break, with the formation of indolent ulcers Some œdema of the ankles and feet is commonly associated.

The plan of general treatment for Raynaud's phenomenon should be followed.

[1] It may be minimized by the use of an emollient (cold cream) or glycerin.

The Effects of Cold

Frostbite.—As its name implies, true frostbite occurs when the skin and possibly deeper structures actually freeze. Usually unclothed parts (fingers, ears, nose) are affected, but even well-shod feet may freeze after prolonged contact with ice or frozen ground. The affected area becomes dead white and hard, and as this transition may not be noticed by the patient, any companion with him must immediately call his attention to such an area.

Preventive Measures include the provision of suitable clothing, constant activity, the avoidance of direct contact with metallic objects and the minimum [illegible]

recovery.

Immersion Foot.—This condition is encountered in those (e.g. shipwrecked seamen) whose feet and legs have been immersed for long periods in water below 15° C.; the hands may also be affected. The parts become numb and swollen, and in more severe cases discoloured, blistered and even gangrenous. Later motor and sensory loss may ensue. Trench foot is an analogous condition which may occur in soldiers occupying waterlogged trenches in cold weather.

Preventive Measures are directed to the maintenance of activity, the avoidance of constricting clothing, and where possible the avoidance of prolonged immersion of the parts. Brisk rubbing is harmful. *Treatment* should begin as soon as possible after rescue. The patient should not be allowed to walk. The body should be kept warm by blankets, but the feet must be kept cool and elevated to reduce swelling; in the often cramped conditions obtaining on rescuing ships, this may be attained by nursing the patient on his face, with the legs bent to right angles at the knees, supported in this position and left outside the bedclothes. On no account should the affected parts be warmed rapidly by the direct application of heat in any form The local treatment of the parts is the same as for frostbite. Even in apparently unpromising cases, loss of tissue from gangrene is often minimal, and even minor amputation should be employed with the greatest conservatism. During recovery adequate relief from pain must be provided.

Chilblains.—A chilblain is an area in which the circulation has been disturbed by cold, often wet cold, in a susceptible individual; the smallest afferent vessels are contracted, the capillaries and smallest efferent vessels dilated. Treatment is largely preventive.

General Measures.—There is no specific diet for chilblains, but an adequate intake of calcium and vitamins, as supplied by a pint of milk and at least one helping of fresh fruit and green vegetables daily, should be ensured. Anæmia, if present, must be corrected and obvious sources of focal sepsis eradicated.

Adequate exercise in the fresh air is of value in the maintenance of an active peripheral circulation.

Drugs —Thyroid extract administered with proper precautions (see p. 354), is beneficial in hypothyroid patients with chilly extremities.

Physical Measures —General irradiation with ultra-violet light appears to

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be

VENOUS THROMBOSIS

Thrombosis in Deep Veins of Calf.—*Preventive Measures.*—In debilitated patients and in previously healthy patients whose treatment requires immobilization (post-operative state, fractures), active exercises, particularly of the legs, should be insisted upon from the first.

debilitated

operative a

thrombosis. *Diagnosis* is of vital importance; it is based upon (1) a rise in pulse rate or temperature which cannot be accounted for on other grounds, (2) the detection of local tenderness in the calf on systematic palpation of the relaxed muscles; later, the tender area may be somewhat swollen and covered with shiny skin under which course distended subcutaneous veins, and (3) the production of pain in the tender area on hyperextension of the ankle joint.

Treatment —In such cases, anticoagulant therapy gives good results. When local signs and symptoms disappear, a supporting bandage is applied and the patient gets up and moves about. When immobilization must be continued, anticoagulants are given for seven days longer, and all possible movements are carried out in bed. In suitable cases the patient leaves hospital about three days after getting up; a support (elastic stocking, or crêpe, Unna's paste or Viscopaste bandage) must be worn for about three months.

Thrombosis of Main Veins.—As soon as the diagnosis is established

block with procaine may be useful in thrombosis affecting an upper extremity but is not advisable in the lower limbs.

Thrombosis in Varicose Veins.—Beginning at some point in the long saphenous system, thrombosis may spread both proximally and distally to obliterate varying lengths of the long saphenous

thrombus The patient then resumes his normal activities. Although under this treatment the process resolves, there is a distinct tendency to recurrence, and the wisest plan is to advise the excision of the involved segments in an interval between attacks, the operation including ligation and division of the long saphenous vein at its junction with the femoral vein.

Migratory Superficial Thrombophlebitis.—This condition is so often

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I. S. R. SINCLAIR.

DISEASES OF THE NOSE, THROAT AND EAR

THE NOSE

INTRODUCTION

CONSIDERATION IS GIVEN in this section to the treatment of th commoner affections of the nose and the nasal accessory air sinuse Surgery plays its own part in connection with these affections, but a such it receives no present attention.

Similarly, lesions of the nose, throat and ear caused by syphilis, tuberculosis and malignant disease are not dealt with; they are more appropriately discussed in the sections set apart for that purpose.

Physiology of the Nose and Nasal Accessory Sinuses in Relation to Treatment

Some knowledge of the physiology of the mucous membrane of the nose and that of the nasal accessory sinuses is essential to the intelligent treatment of diseases of these structures. The chief symptoms are, for the most part, the result of derangement of nasal physiology, and therefore treatment is, in the main, an attempt to restore physiology to normal. The variation from normal may be in any one of the different elements of the nasal mechanism. Mucous membrane, of columnar ciliated type, is the structure upon which function is based. There are slight variations in the membrane in the different parts of the nose, as the more important functions are localized to certain areas. The mucous membrane is rich in glands which secrete the mucus which is essential to the life of the cilia. Under the basement layer of the epithelium is a connective tissue stroma, containing blood vessels and spaces which contain blood. These spaces form the erectile tissue of the nose, and are capable of engorgement with blood or of retraction, according to the functions of the nose in the supply of moisture and warm air to the lung. This erectile tissue is located chiefly in those parts of the nose upon which the air stream impinges—the anterior end of the inferior turbinate, its lower edge and the anterior end of the middle turbinate. This tissue is under the control of the sympathetic nervous system, and derangement of this is responsible for a great many symptoms of nasal disease which call for treatment. Mucus is secreted by the glands of the nose, and thus has functions of its own. As has already been mentioned, it provides a medium in which the cilia of the columnar cells may live and work, and in order that they may carry out their function properly the mucus must be of the correct consistency. The mucus also has the function of protecting the membrane which lines the nose, and its absence or removal is immediately followed by changes in the mucous membrane and by symptoms of nasal discomfort. Particles of foreign material and bacteria inhaled into the nose are caught in the mucus, and are eventually eliminated through the alimentary canal.

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Migratory Superficial Thrombophlebitis.—This condition is so often an early manifestation of thromboangiitis obliterans or of a visceral neoplasm that in all cases a thorough investigation and, if that proves negative, prolonged observation is essential. A felt pad and supporting dressing should be applied over the thrombosed vein. Protein shock therapy by the administration of graded doses of TAB vaccine will occasionally prevent a recurrence of thrombosis, but if the attacks continue long-term anticoagulant therapy should be instituted.

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Principles of Treatment

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Common Nasal Remedies.—These consist of douches, sprays, drops, inhalations, powders and salves of various types. In accordance with the physiological principles which we have enunciated, no remedy which interferes with ciliary function is to be permitted. Therefore any remedy containing drugs in sufficient strength to paralyse or interfere with ciliary activity, as, for example, strong solutions of ephedrine, cocaine or irritants, must be avoided. Ointments or other applications which remain in a thick state within the nose will clog the mucous membrane, and thus prevent ciliary movement. Powders for the most part act as irritants and are not recommended. Douches, when used, must be isotonic, because water tends to paralyse ciliary activity. The main function of a nasal douche is to remove accumulated secretions which coat the mucous membrane and the nasal passages and prevent proper aeration and drainage. By removal of this accumulation the ciliary membrane is given an opportunity to recover, but it must be remembered that, as the function of mucus is to protect the membrane, the repeated and continued use of the nasal douche, by depriving the membrane of its protection, will tend to defeat its own end.

Oily Sprays.—These should be of light oil and, if medicated, must not contain harmful concentrations of drugs.

Drops.—These are more effective than a spray from an atomizer, with which it is difficult to obtain an adequate and even spread of the solution throughout the nasal cavity. They have the merit that they are simpler to use, require less apparatus, and in many cases are all that is required for comfort. Oil should never be used as drops or sprays in young children or infants, owing to the danger of inhalation of the oil and the production of lung complications. Decongestants of many types are available and should be in isotonic solution. Ephedrine is useful and may be used in saline up to 2 per cent. solution. To be most effective, drops should be instilled in the supine position with the head extended.

Inhalations.—Inhalations of steam, medicated with menthol, camphor, eucalyptus, oil of pine or other substance, are frequently used in cases of nasal congestion: they are often of considerable benefit to those suffering from acute congestion of the nose, and the steam forms a convenient vehicle for the application of small quantities of soothing drugs to the mucous membrane. Prescriptions containing these remedies will be found in the Appendix (see p 646).

Other Forms of Treatment.—Certain of these call for mention, since, although outside the scope of medical treatment, they cannot be classified under a surgical heading: they are the galvano-cautery, the use of caustics and sclerosing solutions, ionization and various forms of radiation therapy. These have as their object the reduction of the bulk of the mucous membrane of the nose to provide aeration, or the correction of the sensitiveness of the mucous membrane to particular irritants.

INJURIES OF THE NOSE

Treatment will vary according to the nature of the injury and the problems which it presents. Generally speaking, the conditions calling for attention fall roughly into three categories:

1. Fractures
2. Hæmatomata.
3. Epistaxis

Fractures and Hæmatomata of the Nose.—These are largely surgical problems and their treatment will not be considered here.

Epistaxis.—In such cases two areas of the nose may require treatment.

cocaine hydrochloride solution containing 0 3 ml (5 min) of adrenaline to 4 ml. (1 fl. dr) of cocaine hydrochloride solution. This packing should be left in for a few minutes, and when it is removed, the nose will be found to be comparatively insensitive and further packing of the nose will be rendered very much less unpleasant for the patient. The doctor is able to carry out the packing more thoroughly when the mucous membrane reacts to the cocaine; also the mucous membrane will swell later, and by gripping the pack will increase its efficiency The packing is carried out with 1 in ribbon gauze

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pair of angled forceps it is passed right back along the inferior meatus From the floor of the nose the pack is built up towards the roof, being firmly pushed into all crevices of the nasal cavity In the adult, at least one yard of gauze will be required on each side of the nose In the vast majority of cases this is

out of the mouth The end of the tape is tied to the catheter, which is drawn back through the nose bringing the tape with it, thereby firmly anchoring the pack in the nasopharynx. The insertion of the pack, unless carried out with some degree of skill, is an unpleasant experience for the patient To minimize the

the tape. The tape should be anchored to the face by means of strapping. The packing is then carried out as detailed before, using the post-nasal pack as a base. In this way severe hæmorrhage can be controlled.

Nasal and post-nasal packs should not be left *in situ* for more than two or three days without being changed. Antibiotics should be given to control possible infection of the middle ear via the Eustachian tube.

The Control of Epistaxis by Obliteration of the Bleeding Point.—Cases in which the

method.

nose pack

(5 per cent.) with adrenaline. When this has been left in for a few minutes, the bleeding will be found in all probability to be very much less, and the bleeding veins will be seen to stand out clearly in the mucous membrane of the nose. Obliteration can be carried out either with the actual cautery or with a chromic acid bead. The electro-cautery is used at a dull red heat, and each vein in turn is obliterated with the point of the cautery, the cauterizing being made as

acid are picked up on the point of the probe. The flame is then applied to the probe a short distance above the crystals. After a moment or two the crystals melt, and run down to form a drop on the point of the probe. As soon as the

General Treatment

Brisk nasal hæmorrhage is frequently an alarming experience for a patient, and it is very often wise before commencing treatment to give the patient an injection of morphine or other sedative This will help in many cases to control the bleeding by keeping the

tions very much easier for the

hæmorrhage as the result of

treatment of epistaxis in these cases, apart from the purely local measures detailed above, belongs properly to the sections in which these diseases are found

AFFECTIONS OF THE NOSE

Rhinitis.—*Acute Rhinitis* (See Coryza, p. 650)

Purulent Rhinitis.—*This form of infection is most frequently seen in con-*

virulent infection of the mucous

ith douches and ordinary cleanli-

nent of the diseases during the

may include *the administration*

of penicillin

Membranous Rhinitis.—As this condition is most frequently due to the Klebs-Loffler bacillus, the treatment is the same as in cases of diphtheria Other forms of membranous rhinitis are found in patients suffering from marked debility, and in such cases they may be treated with mild alkaline douches, instillations of drops, such as mild silver protein (B.P.C.) (10 per cent.), silver

protein (B P.) (10 per cent.), and other non-irritant applications. (For prescriptions, see Appendix, p. 646.)

Chronic Rhinitis.—The treatment of chronic rhinitis depends to a considerable extent upon the stage to which the chronic condition has advanced. In the earliest stage the return of comfort to the patient depends upon the restoration of ciliary action, and as this is prevented by the want of proper aeration in the nose and the clogging of the mucous membrane with thickened secretions, treatment should be directed towards the relief of this condition, and alkaline douches

should be avoided.

mucous membrane, and this, therefore, will entail operative procedures.

certain amount can be done to moisten the thin and dry nasal mucous membrane, but, except in the *earliest stages*, the condition cannot be cured and even then can only be checked.

The removal of the crusts is best carried out by means of douching, with or

should douche the nose with a weak saline solution, e.g. 1 teaspoonful of salt to a pint of warm water. Where the crusting is not heavy and the condition is in the earlier stages, the nose should be douched with mild alkaline solution (see Appendix, p 646)

The nose can be douched morning and night, but, if douching once daily is sufficient, cleansing should be confined to this one occasion. Excessive douching is apt to lead to irritation and further discomfort. After douching, the nose should be sprayed with an oily solution. A light oil is best for this purpose and may contain some essential oil to render the odour pleasant. This helps to protect the mucous membrane and also tends to delay the formation of crusts.

Another form of treatment consists in spraying the nasal cavity with œstradiol in oil (0 5 ml of a solution containing 5 mg. per ml is sprayed into each nostril)

once in a fortnight. In favourable cases it can be omitted altogether. It is essential for the success of this treatment that cleansing of the nasal mucous membrane should be meticulously carried out. This is done by douching, as

described above, and if necessary in the earlier stages, by picking out the crusts under direct vision.

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above.

Nasal Polypi.—The treatment of nasal polypi is symptomatic only, in so far as this section is concerned. A careful search must first be made for the underlying cause, and the method adopted will depend upon what is discovered. Treatment may be instituted, for example, on account of an allergic basis for the polypus f

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occur.

Tuberculosis and Syphilis.—These conditions are fully dealt with elsewhere and need not be mentioned here (see pp. 122, 184).

Nasal Allergy.—The question of allergy is also considered on p. 695 and antihistamine drugs may be of great value. Local treatment, however, may be called for in the nose. Ephedrine is the most useful drug in such cases. Ephedrine is applied preferably in the form of drops in normal saline solution (0 5 or 1 per cent.).

Zinc ionization will in many cases give comfort to the sufferers from nasal allergy. It has been used to a great extent in cases of specific nasal allergy, as, *for example*, hay fever, but is also of value *in the non-specific types of sensitivity,* such

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will facilitate manipulation and by the shrinkage of the mucous membrane will render the removal of the foreign body a comparatively simple matter. In the case of a small child, the patient must be controlled by another person, preferably not the mother, and it is useless to attempt the removal of the foreign body unless the assistant is capable of holding the child perfectly still. It may be necessary, in cases of doubt, to give an anæsthetic in order to make a complete *examination of the nasal cavity. An anæsthetic in such cases should never* be given without adequate preparation, for the child is frequently frightened and resistive, and, as such, may make an extremely bad subject for anæsthesia. When an anæsthetic has been given, a finger should be inserted into the nasopharynx and placed in the choana of the nostril which is being examined, as it is possible to push the foreign body backwards into the nasopharynx, whence it may be either inhaled or swallowed The finger in the nasopharynx

concretion. These concretions may be very large, and it may be found advisable to break them up before removing them.

SINUSITIS

Acute Sinusitis.—In the treatment of sinusitis the aims are similar to those in affections of the nose, namely, the relief of pain and the restoration of function. The loss of ciliary function for a prolonged period may render treatment unavailing. If, therefore, surgical treatment is to be avoided, the early stages of the physiological derangement must not be neglected. As pain is so frequently the result of obstruction to drainage, the relief of pain in many cases becomes the problem of securing the release of contents obstructed within the sinus. As the sinus can only drain through the small ostium into the nasal cavity, treatment is primarily directed towards restoring the patency of the ostium. Agents are used which have the function of shrinking the mucous membrane of the nose. Of these, the simplest are steam inhalations containing menthol, which not only help to shrink the mucous membrane but also have an analgesic action and will relieve the accompanying discomfort. Ephedrine (1 to 2 per cent) in isotonic saline solution or other decongestant may be instilled into the nose. This will help to shrink the turbinates and will open up the œdematous middle meatus. These drops can be repeated at sufficiently frequent intervals to maintain a shrunken condition of the nasal mucous membrane, and may thus promote a flow of secretion from the sinuses. Rest is of the utmost importance in the treatment of sinusitis, and a patient should always be advised to refrain from business or other activity, since return to health will be delayed if he insists on carrying on with his daily work. Another essential is that the patient should remain in the same temperature as far as possible, to prevent changes in the tension in the nasal mucous membrane. Accordingly, rest in bed is generally advisable, as this provides the easiest method of controlling the patient's activity; and should there be any constitutional disturbance, this must be insisted upon. For the pain itself, apart from analgesic drugs and measures which aim at the relief of tension within the sinuses, the application of heat in various forms is the most valuable way of relieving the patient. Radiant heat baths or short-wave diathermy may bring about an immediate improvement, but on the other hand, by increasing congestion, they may cause greater pain. In such cases the heat should be immediately discontinued. Short-wave diathermy as a rule is most useful in the subacute stages when the sinusitis is beginning to abate.

In the purulent stage of the infection, where there is considerable constitutional disturbance, the object of treatment should be to avoid operativ interference if that be possible. Surgical measures should be reserved until th acute stage has passed. It may happen, however, that increasing severity o symptoms, such as swelling or increase of pain, may render it necessary undertake some operative measure for the relief of the patient. Proof-punctu permits lavage, or indwelling catheters can be introduced through wh treatment is continued. Proof-puncture, however, in the stage of ac inflammation may be extremely painful, so that the question of anæsthesia, lo or general, must receive careful consideration. This procedure has its grea value where the sinus is filled with purulent fluid. In many cases of the r acute type, however, there is no cavity within the sinus, the whole space b occupied with œdematous mucous membrane. In which case proof-punc will accomplish nothing except as a means of introducing penicillin int

sinus. Procaine penicillin in oil is the most effective preparation in these circumstances. Each case must be judged by the individual *reaction to the* procedure, but as a rule it should not be repeated
after three or
that proof-pu
considered

Chronic Sinusitis.—In chronic sinusitis it is frequently worth while to attempt to clear up the inf

before treatment is finally decided upon. Where gross infection is shown by radiography, and where there is obviously polypus formation within the sinus, then conservative measures are not likely to achieve cure and recourse must be had to surgery. Where, however, the infection is not severe, proof-puncture and lavage with saline solution may be sufficient to allow the cilia to recover function.

The displacement method of introducing agents within the sinuses is a useful one. It consists of applying suction to the nose in such a way that when the head is placed in a suitable position the ostia of the sinuses are submerged in the solution which is being introduced The air is drawn out of the sinus by the suction, and the drug allowed thereby to find its way in Ephedrine in saline (½ per cent) is frequently used in this way, by its gradual elimination it gives a prolonged action and keeps the ostium shrunk, thus allowing drainage over a considerable period Short-wave diathermy

which require treatment are osteomyelitis, abscess formation in the tissues outside the sinuses, such changes in the eyes as are induced by pressure either upon the orbit or upon the optic nerve, and meningitis. This last is a late complication due to extension of the disease. The treatment of these complications of sinusitis is mainly palliative, pending the arrival of surgical assistance (see also Penicillin, p. 64)

THE PHARYNX

TONSILLITIS

Acute Tonsillitis.—
to which the illness has pr
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abort the disease. But it must be impressed upon the practitioner that this condition must never be treated as of small consequence, and fairly stringent

s therefore unwise to increase fluid loss by excessive purging. Where there is rise of temperature, antifebrile drugs may be used, such as aspirin. Treatment with sulphonamides or antibiotics is fully discussed elsewhere (see p. 57). The local treatment consists chiefly of gargles and paints, which should be of a mild nature There should be no nipping or burning with any of the drugs used. The mucous membrane is in an inflamed condition and requires soothing and not irritation. A gargle of carbolic acid, sodium sulphocarbolate, sodium bicarbonate and glycerin (see Appendix, p. 647) may be used. Boroglycerin is a good paint for early acute cases There may be, even in the earliest stages, a marked glandular involvement The glands of the submaxillary and upper cervical region may be tender and swollen, limiting thereby the movements of the neck. These conditions may be met by hot applications which give relief and also reduce swelling.

In the follicular stage of tonsillitis, in which the tonsils are found to be spotted, treatment is frequently simpler, as at such a stage the patient is usually quite willing to retire to bed. The symptoms are rise of temperature and of pulse-rate, with associated pain and difficulty in swallowing This may be so severe as to determine the nature of the patient's diet, confining it to ice-cream, junket, strained soup and porridge, and to fluids such as tea, barley water, glucose and orange juice. Locally, gargles and paints are again required, and treatment of the glands of the neck should they be enlarged and tender.

In the membranous form of tonsillitis there is an extension of the infection from the above stage, and treatment has to be correspondingly energetic. The patient's general condition as a rule is weaker and his fluid intake is usually considerably limited owing to the extreme pain in swallowing In such cases, if the patient does not seem to be taking sufficient liquid by the mouth, it must be given in other ways This may take the form of a rectal saline, but the best method is the intravenous administration of glucose (5 per cent) in normal saline by the continuous-drip system In this stage of the infection, gargles are frequently ineffective, as the patient may lack the strength to use them. The membrane also frequently covers parts of the throat to which the gargle does not reach. Under these circumstances an antiseptic spray may be the best means of cleansing the infected parts. The spray may consist of hydrogen peroxide and water, in equal parts, or a solution of glycerin of thymol (see Appendix, p. 646) Warm irrigations are another useful and soothing method of treatment. Soothing paints also are excellent, because they help to ease the local condition and stimulate swallowing and the flow of saliva Inhalations may be required because the inflammation is seldom localized and there is frequently hyperæmia of the larynx A useful inhalation consists of 15 to 20 drops of compound tincture of benzoin (Friar's balsam) in 1 pint of hot water.

It is important to maintain as much movement as possible in the throat and to keep the surfaces constantly cleansed It is for this reason that sprays are of such value, for, even if the saliva is deficient, they induce swallowing movements or the coughing up of infected material In children, especially, the spray is useful when the throat becomes really sore. A child sometimes refuses to gargle or drink, and it is in these cases that the greatest danger occurs from dehydration. Further, the throat is held completely quiet so that the infection becomes severe and there is little or no cleansing of the parts locally. In order to spray the throat, a certain amount of restraint may be required to control the child properly, and, as it is unlikely that the mother will be able to carry out this

treatment adequately, it is usually best to have these cases under the charge of a nurse or to place them in hospital. An excess of affection has before now been responsible for tragedy in the case of a child.

Complications.—Of the complications of tonsillitis, peritonsillar abscess or quinsy is the most frequent. In the early stages, in which the tonsillar region is slightly swollen and the soft palate is showing only a little sign of œdema, palliatives are indicated, such as frequent hot gargles and fomentations to the glands. Sleep is usually interfered with, and it is an excellent thing to give a sedative at night in order to conserve the patient's strength. The systemic administration of penicillin at this stage frequently causes regression of the inflammation without the formation of pus. The question frequently arises as

cases are seen only when there is an obvious bulge in some part or other of the swollen soft palate. In such cases it is a simple matter to push a pair of blunt forceps into the soft swelling and evacuate the pus When, however, no point of softening exists, the peritonsillar abscess is best opened from the superior tonsillar crypt. A long pair of blunt-pointed forceps is used. If desired, the

the superior tonsillar crypt and pushed sharply upwards and outwards through the capsule into the abscess cavity, and widely opened. This is followed by a

Abscesses may occur in other parts of the throat as the result of tonsillar infection. These are more frequent in young children. They occur either in the nasopharynx or in the hypopharynx, and their treatment demands evacuation at an early stage of the infection. Correct treatment is of the utmost importance, and the possiblity of this affection being present should never be lost sight of in unexplained illnesses in young children, where there is difficulty in breathing or swallowing In all cases of acute tonsillitis and its complications, when general infection is marked, the use of sulphonamides or antibiotics is of the greatest value in re

Chroni comparative frequency hese patients are symptom-free, because they have acquired immunity to their infection, and it is not until some general infection, or lowering of resistance, causes a breakdown of the immunity, that symptoms appear which *demand attention.* The use of palliative treatment in such a case is to enable the immunity to be built up again.

Palliative treatment may consist of painting the tonsils ; in cases of chronic tonsillitis such paints are of a faintly irritating character, the commonest of these being Mandl's paint. Gargles may be recommended, as they serve the purpose of exercising the pharyngeal muscles and ensuring an adequate blood supply to the parts concerned. In such cases, also, suction is recommended as likely to remove the debris and infected material from the tonsil and, no doubt,

as far as the surface is concerned, it will do so. But a consideration of the anatomy of the tonsil will suggest very strongly that the tortuous channels of small size which constitute the crypts are not likely to be adequately evacuated by any method of surface suction. Radiation of various kinds has been used in tonsillitis,

been established over a prolonged period, with the usual fibrous tissue formation and replacement of columnar epithelium with other forms, such treatment is unlikely to reverse the established pathological changes. Gamma radiation has been recommended for treatment in inflamed tonsils, and there is no doubt that radiation will remove tonsillar tissue if used in sufficiently large doses. But it is equally evident that if used in sufficient dosage to destroy the tonsil, the side-effects are such that the treatment does not justify the expenditure of the time and money required. Either the reactions are severe—very much more so than with a simple tonsillectomy—or the treatment is so prolonged that the expense will be a very serious consideration

The technique of removal of the tonsils does not fall within the scope of this section, but the practitioner may have to make the decision as to when the tonsils should be removed, and to know the appropriate method. Operations for

completely by diathermy coagulation The coagulation technique has not proved as popular or successful as was expected from the claims which had been made for it. The complete removal of the tonsil by coagulation involves some half a dozen sittings and occupies a considerable period of time.

anæsthetic and to the psychological upset inseparable from the idea of an

operation and can be applied in cases where the physical state of the patient

the deeper structures of the throat are left unharmed. The treatment tends to be lengthy and is frequently more painful than those carrying it out are wont to admit.

PHARYNGITIS

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patient's habits, surroundings and type of work. Habits, particularly with

regard to smoking and alcohol, require investigation. The presence or absence of gastric trouble, rheumatism and like diseases may modify the attitude towards treatment. Excessive dust or a special type of atmosphere may be found to be of ætiological importance. For instance, the presence of ammonia fumes or other forms of irritant may require to be eliminated before treatment can be successful. Inflammation

be expected in the pharynx. Treatment of chronic tonsillitis may be necessary, though it should be noted in this connection that the removal of tonsils for the cure of pharyngitis should not be undertaken, except after most careful consideration, as in most cases the tonsillectomy will tend to aggravate the chronic pharyngitis rather than to improve it.

The local treatment of pharyngitis depends upon whether the condition is acute or chronic. Gargles are rarely of value in *an acute pharyngitis*, apart from helping the flow of saliva and assisting in the lubrication of the mucous membrane. Sprays and paints of boroglycerin or glycerin and tannin are of real value. Steam inhalations are soothing in the more severe types of case. These may be medicated, as, for instance, with Friar's balsam. Lozenges containing menthol or other drugs are soothing to the patient. Where inflammation is severe, saline irrigations should be employed. Inflamed and tender glands require treatment by fomentations or other form of heat. Sulphonamide or penicillin therapy should be instituted immediately. In the *chronic stage*, treatment is more of the nature of counter-irritation, and such application may be made to the pharynx locally as will help to stimulate the resolution of the inflamed mucous membrane. Paints, such as Mandl's paint, or the careful touching of the inflamed portions of membrane with iodine or with silver nitrate (10 per cent), will help to reduce the irritation. The cautery or diathermy,

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after which the fine cautery point may be used very sparingly on the enlarged lymph nodes

Retro-pharyngeal Abscess.—The difficulties caused by retro-pharyngeal abscess are chiefly those of diagnosis : but where obstruction of the nasopharynx or larynx is being caused by abscess formation, the relief of the obstruction is the treatment immediately required The abscess, if causing obstruction, must be opened, and this may be done by the oral route, except in the case of abscesses which have their origin in tuberculous cervical caries.

NEUROSES OF PHARYNX

Sensory Neurosis.—Paræsthesia, or the underlying cause of paræsthesia,

are cancer-phobes, and in such cases one of the most important parts of the treatment is the suggestion to the patient that there is no underlying disease and that a little local treatment is probably all that is required.

Anæsthesia of the Pharynx.—This condition usually accompanies lesions of the base of the brain, and therefore is not amenable to treatment.

Glosso-pharyngeal Tic.—The treatment of glosso-pharyngeal tic falls into the category of surgical treatment and consists of nerve section

PATERSON-KELLY SYNDROME (PLUMMER-VINSON)

The symptoms of dysphagia will usually clear up rapidly under appropriate treatment for the associated anæmia (see p. 402 *et seq.*). Only when these measures are unsuccessful does local treatment of the obstruction become necessary. This consists in stretching the stricture through a laryngoscope or œsophagoscope. The blind intubation of these patients is to be deprecated, and in the first instance, treatment should be carried out under direct vision by those experienced in such procedures

THE EAR

DISEASES OF THE EXTERNAL EAR

The Auricle.—*Injuries*—Hæmatoma of the auricle calls for treatment on

ichthyol and glycerin soak (10 per cent)

Perichondritis—When inflammation has supervened, treatment consists in

incision as far as possible, but where the furuncle is very large and pus has obviously formed, then incision may be undertaken.

Otitis Externa.—The treatment of otitis externa varies according to the stage of the disease and its particular type. In many of these cases the ear is filled with discharge and debris it may therefore be essential to cleanse it by syringing. If possible this course should be avoided, and if syringing has to be resorted to, the ear should be carefully dried afterwards

In the very acutely inflamed type, where there is some perichondritis, the treatment should be the same as that outlined for furunculosis. When the most

Wax in the Ear.—Wax in the ear is removed by syringing. Where the wax is very hard, it should first be softened by the instillation of drops of saturated solution of bicarbonate of soda. Half a dozen drops of this should be instilled four or five times for one to two d

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Warm water, preferably boiled, is quite effective, or tap water with a few drops of antiseptic added may be used. The patient should be instructed to hold the basin or kidney-dish underneath the ear to catch the

which fits around the ear

Unless the person carryi

sharp nozzle should not

The stream of water should be directed against the posterior superior aspect of the meatal wall. By doing so the plug of wax is loosened and the water passing behind the wax tends to force the plug outwards. Great force must not be used, and if considerable difficulty is being experienced, it will assist if the posterior edge of the wax plug be elevated from the meatal wall to make a point of entry for the stream of water. During the syringing frequent inspection of the meatus should be made in order to ascertain the progress of the removal

After the plug of wax has been removed the ear should be dried of excess fluid If, as sometimes happens, some epithelium is removed along with the wax and a raw place is left on the meatal wall, it is wise to pack the ear with a strip of gauze soaked in aluminium acetate solution (8 per cent.) for twelve hours to prevent the possibility of infection Where there is known to be a perforation in the drum, wax should not be removed by syringing, but preferably by being picked out if necessary after softening. Where there is a perforation of the drum there is a possiblity of the water passing through into the middle-ear cleft and

destruction by pressure. The hardness of the plug may be such that a general anæsthetic may be required to accomplish its removal.

Foreign Bodies in the Ear.—From the point of view of treatment, foreign bodies in the ear may be divided into three classes—vegetable, mineral and animal.

Vegetable foreign bodies, e g a pea, should not be removed by syringing. If the initial syringing is unsuccessful, the foreign body will swell with the

etc., is required for their safe removal. Insects and such animal foreign bodies should be killed first by the introduction of spirit drops or chloroform vapour, and then syringed out. In small children, anæsthesia is frequently required for the safe removal of the foreign body. It is useless to attempt to remove a foreign body from the ear of a kicking, struggling child. In such cases the

AFFECTIONS OF THE DRUM

Rupture of the Drum.—Whether this occurs as a result of a concussion, for example from a blow or gun-fire, or from a fracture of the skull, the main principle of treatment is inactivity. A piece of sterile wool should be inserted in the meatus and no syringing or cleansing of any kind permitted. The prophylactic use of penicillin or the sulphonamides will help to prevent suppurative complications. In cases where rupture has taken place and suppuration, as may frequently happen, sets in, then the treatment is the same as that of conservative treatment for acute otitis media, to which the reader is referred.

Myringitis Bullosa.—Very large hæmorrhagic blisters may occasionally be

prevent middle ear infection and its complications.

Herpes.—Herpes of the auricle and meatus may occur as part of herpes zoster oticus (Hunt's disease) The local condition is treated as in otitis externa, the chief symptom requiring attention being pain.

DISEASES OF THE MIDDLE EAR

Acute Otitis Media.—In acute otitis media treatment is required on account of pain, deafness, discharge from the ear and constitutional disturbance. The condition, from the point of view of treatment, falls naturally into two sections: firstly, treatment of acute otitis media before discharge appears in the ear: and,

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stretched drum membrane, direct application to the inflamed membrane may be made by means of anæsthetic drops. One of the most useful forms of application is anhydrous glycerin containing 4 per cent. carbolic acid Heat is a favoured form of application, and warm drops of oil have been used traditionally as a

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temperature

channel—the Eustachian tube. Once discharge is established, nature must be assisted in drying up the secretions.

In the early stages of copious discharge, cleanliness of the ear is essential. This can be accomplished by frequent mopping of the ear with cotton-tipped applicators, or if the ear becomes clogged with discharge, a few drops of peroxide of hydrogen (10 volumes) should be instilled and the ear syringed gently with a

treatment. After the ear is dry, the hearing in the majority of cases is subnormal and inflation of the Eustachian tube will do a considerable amount towards restoring it to normal and, in many cases, will prevent permanent deafness. This inflation should always form the last step in the treatment, and must never be neglected.

Indications for Paracentesis —Although paracentesis is a surgical procedure, it must sometimes be undertaken by those who are at a considerable distance from hospital service, and it is therefore essential that the medical practitioner undertaking the treatment of acute otitis media should have a clear idea of the conditions which demand this procedure. One of the first effects of an acute

toxæmia with obvious middle-ear infection and the tympanic membrane is bulging, relief may be expected by the release of the contents of the middle ear. Again, if a drum is evidently upon the point of perforation, indicated by a yellowish area appearing at the most prominent part, immediate relief by paracentesis may obviate the sloughing of the drum membrane; a surgical cut so made will heal rapidly, causing less permanent damage to the drum structure than if a portion of the membrane is allowed to slough out. Where deafness is becoming more marked, owing to increasing tension in the middle ear, paracentesis may afford the most certain method of ensuring rapid and complete return of hearing.

In the treatment of these cases of acute middle-ear infection, one principle must always be observed, viz. that treatment is to be directed towards the prevention of deafness: little or nothing can be done for a patient once the hearing has been lost for a period. In this case above all others, prevention is better than cure.

An adequate source of light is required to carry out paracentesis This may be obtained either from an electric lamp, the light from which may be focused upon the ear by means of a head-mirror, or it may be obtained from an electric auriscope. Before carrying out a paracentesis the ear must be cleansed thoroughly and completely so that a clear view of the drum-membrane is obtained. General

anæsthesia is advisable in all cases. When the patient has been properly anæsthetized, a paracentesis knife is introduced and the drum is incised in the posterior half in the form of a J the upright portion commencing a little below the posterior horizontal fold of the drum and the incision being brought round in the lower part to finish just below the handle of the malleus. This procedure must, of course, be carried out with proper aseptic precautions, and the after-treatment is that for discharging ear.

Complications of Acute Otitis Media.—Treatment of complications of acute otitis media is essentially surgical, though chemotherapy and the use of antibiotics are important and indispensable adjuncts.

Chronic Otitis Media.—Treatment of this condition depends to a great extent upon the type of suppuration, the part of the ear cavity which is affected, the duration of the condition and the presence or absence of bone disease. It is obvious, therefore, that an adequate knowledge of the state of affairs in the middle ear is essential for the proper planning of the treatment. In the consideration of such a case the circumstances of the individual must not be overlooked, and treatment should be selected with regard to these circumstances, as, for instance, the patient's means and the conditions of his work.

The treatment of chronic otitis media has three chief aims, of which the first [illegible] reduce to a minimum the loss of working time. Both surgical and conservative treatment play a part in the cure of chronic otitis media. Surgical treatment is essential in the presence of certain complications, such as brain abscess, labyrinthitis, necrosis of bone and extensive cholesteatoma formation. The selection of the type of operation will fall upon the surgeon, who will make his decision in view of the conditions present and in keeping with the principles which have just been laid down

Conservative Treatment.—This must be regarded as the method of choice. [illegible] are instilled into the ear; and, thirdly, special forms of treatment may be used. To cleanse the ear, peroxide of hydrogen drops may be instilled in order to loosen any accumulated debris This should then be syringed out with boric [illegible] being carried out, should form the last stage of the treatment. In certain cases attempts have been made to introduce agents via the Eustachian tube, such as

mild silver protein (B.P.C.) silver protein (B.P.) and oils of various kinds. In addition, powders are used with the object of drying up the ear. The simplest

they are most useful during the later stages of treatment, when the ear is almost dry. A large quantity of powder should not be used, but only sufficient to produce a satisfactory coating. The use of antibiotics in chronic otitis media has proved very disappointing and may even be harmful.

Special forms of treatment are sometimes used, as, for instance, ionization In some hands this treatment gives beneficial results. It consists in passing an electric current through the ear, using zinc as the positive pole in the ear. The application of the zinc is carried out by filling the ear with zinc sulphate solution,

This is done either by massaging the solution into the ear, to exclude air bubbles, or in certain cases where a perforation exists, a cannula is used to introduce the solution into the middle ear. Current to the extent of 5 mA is used for ten to twenty minutes. Three or more applications may be required to obtain a good result. This treatment is particularly useful in young people, such as school-children, but is quite useless where extensive disease exists, in particular bone

for treatment of these conditions—stapes mobilization and fenestration Mobilization aims at breaking down the otosclerotic bone uniting the stapes to the oval window, while the fenestration operation aims at restoring mobility

The mobilization technique is simpler than the fenestration operation and is therefore used in doubtful cases or as a preliminary to the fenestration. The most suitable patients for this treatment are young people under thirty years of age with normal tympanic membranes and deafness of pure middle-ear type. The contra-indications to it are the presence of nerve deafness, past or present suppuration in the middle ear and extreme degrees of deafness. As only a limited amount of hearing can be restored by operation, the improvement so obtaine

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cases tr

age advances the presence of senile nerve deafness progressively limits the advantages which can be obtained. Patients over fifty years of age are usually unsuitable subjects for operation.

can restore hearing to its former level.

Deaf Aids

When we are unable to prescribe treatment which will cure patients of the foregoing forms of deafness, we can still do something to assist them to hear, so the practitioner is often asked for advice regarding artificial aids to hearing A knowledge of such instruments is therefore essential to every practitioner

There are two chief classes of aid—the mechanical and the electrical. The first group includes the familiar ear-trumpet, auricles and artificial drums. The second includes electrical and valve instruments. The advantage of the mechani-

hearing-aid, is so conspicuous that many patients refuse to use it The auricle is, in effect, a miniature trumpet or shell which collects the sound and transfers

the deficiency in the drum-membrane In certain instances they do excellent service.

Of the electrical aids, from the point of view of performance, the valve instrument is very much superior to the old non-valve telephone type. The

be obtained on approval for adequate trial at home before it is finally purchased. This will entail a small fee, which will be deducted from the purchase

price if the instrument is retained. All the firms on the register of the National Institute for the Deaf will make this concession. The price of these instruments will vary from a matter of shillings in some of the non-electrical types to over £20 for the more elaborate instruments.

THE LARYNX

LARYNGITIS

Acute Laryngitis.—This condition is usually part of a general infection of the upper air-passages, and treatment of laryngitis in a great many cases must [illegible]

chronic laryngitis. One of the commonest causes of acute laryngitis is the use of the voice in the presence of an inflammation of the upper air-passages. Resting the larynx involves not only the avoidance of vocal function but also the avoidance of muscular effort. As a considerable muscular effort is required from the larynx every time the thorax is braced or the arms used vigorously, [illegible]

the further advantage that the patient is kept in an even temperature, which is another important point in treatment

General febrile conditions will be met by antifebrile measures, laxatives, etc., as for coryza. Locally the inflamed larynx must be soothed. This may be done by steam inhalations, sprays and direct applications. Steam inhalations may be medicated by the addition of soothing agents. Compound tincture of benzoin is one of the most useful of these: 15 to 20 drops should be placed in [illegible] steam inhaled for fifteen minutes at a time. [illegible] to the larynx by means of a dressed probe

Frequently there is acute pain in the neck, and applications of heat—kaolin poultices, thermal pads, etc.—give comfort and relief.

Chronic Laryngitis.—The first step in the treatment of a chronic laryngitis consists in systematic search for the exciting agent. The removal of the cause of the irritation is essential. If it is impossible to identify any one cause, then all sources of irritation must be eliminated, such as tobacco, alcohol, the presence of fumes, frequent contact with dust, etc. The voice should be put at rest for a period, provided the patient's economic condition will permit. Inhalations of compound tincture of benzoin should be prescribed to be used at night-time only, and a soothing spray can be used frequently throughout the day

Locally the larynx can be painted with mild preparations, and in very chronic and resistant cases a weak solution of silver nitrate (2½ per cent.) or zinc sulphate (5 to 10 per cent.) may be tried. This, however, must be used with the utmost care. Complete examination of the upper respiratory passages must always form part of the preliminaries to treatment, as a sinusitis or other infection may be found which will require treatment before any improvement can be expected in the laryngeal condition.

If it is possible to change the patient's environment, this is frequently a

valuable measure, and in such circumstances warm, south-westerly exposures should be chosen.

ŒDEMA OF THE LARYNX

[illegible]

inflammation. This may be due to a variety of causes such as diphtheria, primary septic infection of the larynx, abscess or infection of the respiratory tract above the larynx, chronic disease around the larynx, or reactions to trauma [illegible]

service. It must also be remembered that severe dysphagia may limit the patient's fluid intake and thereby increase toxæmia. In such circumstances [illegible]

urticaria, drug reactions and certain systemic diseases such as nephrosis, attention must be directed to the primary disorder In acute urticarial œdema subcutaneous injections of 0 3 to 0 5 ml (5 to 8 min.) of adrenaline usually bring rapid relief Locally a spray of 1 in 1,000 adrenaline solution, with or without the addition of 10 per cent cocaine solution, is helpful If the necessary instruments are available, scarification or puncture of the ballooned tissue may be undertaken in severe cases In less urgent cases the use of antihistamine drugs is the treatment of choice

When conservative measures have failed, it becomes necessary to resort to intubation or tracheotomy The point at which such treatment is demanded depends partly on the rapidity of progress of the œdema and partly on the response of the patient's circulation to the increased strain upon it A rising pulse rate is always a danger sign, and if, in an afebrile adult, the pulse exceeds 100, preparation should be made for intubation or tracheotomy. The method chosen will depend on the cause of the œdema . if rapid recovery can be anticipated, as in urticarial œdema, then intubation with a soft rubber tube is the method of choice , but if, owing to inflammation or some other cause, immediate recovery cannot be expected, then tracheotomy is necessary It should be emphasized that tracheotomy should not be delayed until it is a final desperate measure to save life, but should be undertaken as a deliberate surgical procedure. In many cases of inflammatory origin the relief of obstruction to the airway is not [illegible] may be decisive in the patient's favour

APPENDIX

NOSE

℞	Sodium Biborate	
	Sodium Bicarbonate	
	Sodium Chloride . .	āā 8 g. (2 dr.)

Sig.—One teaspoonful to a pint of warm water.

℞	Menthol . .	0·5 per cent.
	Oil of Lemon . . .	0·5 per cent.
	Liquid Paraffin	30 ml. (1 fl. oz.)

Sig.—Use in an atomizer.

℞	Ephedrine Hydrochloride	1 to 2 per cent.
	Glucose .	4 per cent.
	Normal Saline . .	30 ml. (1 fl. oz.)

Sig.—Use in an atomizer.

EAR

℞	Solution of aluminium acetate . .	30 ml. (1 fl. oz.)

Sig.—Soak $\frac{1}{2}$ in ribbon gauze in solution and pack into the ear once daily.

℞	Ichthammol in glycerin, 10 per cent .	30 ml. (1 fl. oz.)

Sig.—Soak $\frac{1}{2}$ in. ribbon gauze in solution and pack into the ear once daily.

℞	Resublimated Iodine .	0·75 per cent.
	Boric Acid Powder	30 g. (1 oz.)

Sig.—Use in a powder-blower as directed.

℞	Boric Acid . .	1 g. (15 gr.)
	Rectified Spirit	30 ml. (1 fl. oz.)

Sig.—Ear drops.

LARYNX

℞	Compound Tincture of Benzoin	30 ml. (1 fl. oz.)

Sig.—15 to 30 drops in a jug of hot water for an inhalation.

PHARYNX

℞	Sodium Bicarbonate .	2·5 g. (40 gr.)
	Compound Solution of Thymol	30 ml. (1 fl. oz.)
	Glycerine	30 ml. (1 fl. oz.)

Dilute eight times with water

Sig.—The throat spray or gargle, to be used as directed

℞	Phenol.	
	Sodium Sulphocarbolate	
	Sodium Bicarbonate . . .	āā 15 g. (½ oz.)
	Glycerine	150 ml. (5 fl. oz.)
	Solution of Carmine . .	0.3 ml. (5 min.)
	Orange Flower Water . . .	120 ml. (4 fl. oz.)

Sig.—Dilute with an equal quantity of water and use as a gargle.

Mandl's Paint

℞	Iodine . . .	0.3 g. (5 gr.)
	Potassium Iodide .	1.5 g. (25 gr.)
	Peppermint Oil	0.3 ml. (5 min.)
	Glycerine . .	30 ml. (1 fl. oz.)

Sig.—Use as a paint as directed.

J. S. HALL

DISEASES OF THE RESPIRATORY SYSTEM

THE PREVENTION OF ACUTE RESPIRATORY INFECTIONS

THE MOST COMMON predisposing causes of the more severe respiratory infections, such as bronchitis and pneumonia, are coryza and influenza. This is particularly the case when infection occurs in persons whose resistance is lowered from any cause. It is for this reason that we believe that in the field of prevention, education of the individual sufferer from the common cold is of prime importance. People who are infected should, particularly during the first twenty-four to forty-eight hours of the disease, isolate themselves in their homes, or, failing this, refrain from entering places of public entertainment such as cinemas and theatres, where people are crowded together. They should keep away from non-infected persons. It may be necessary to remind them to use a handkerchief when coughing and sneezing, and so avoid spraying their neighbours with infected droplets.

It should be explained to persons in the acute stage of coryza that isolation at home is not merely a social obligation required for the prevention of infection of others, but that resting in a room at a fairly constant temperature is the best means of obtaining a rapid cure and limiting the liability to more serious disease from extension of the inflammation

During

for certain

This advice

cardiac and pulmonary disease and, in particular, those with chronic bronchitis,

their patients, especially infants and debilitated persons.

Lastly, early and adequate treatment of measles and whooping-cough in infants and young children is important if complications such as severe bronchitis and pneumonia are to be prevented

Under ordinary living conditions few people can hope to avoid infection at some time during the winter months. Every effort should be made to improve the health and raise the general resistance of persons who are peculiarly susceptible, or who have chronic organic disease, by giving common-sense advice on the following points.

1. The avoidance of excessive mental or physical fatigue.
2. The avoidance of undue exposure to wet and cold, by staying indoors

if it is both cold and foggy.

e harmful. On the contrary,

cise, so long as it is within the

limits of the patient's tolerance, is one of the most important factors calculated to improve the general health. The beneficial effects of fresh air can be continued at night by insisting that bedroom windows be kept open. In addition, in

schools and institutions where there are dormitories, the beds should be spaced at least 7 ft. apart.

ness to suit the climatic conditions. Wet and therefore cold feet, especially if endured for hours while working, are a potent factor in lowering the vitality, often with serious consequences. The obvious preventive measure is the use of stout footwear. Health as well as comfort may be dependent on having a dry pair of shoes and stockings available at the place of work.

Since chronic irritation of the air passages predisposes to infection, attention should be directed to the irritation produced by an atmosphere of cigarette smoke. In certain cases it may be necessary to prohibit or at least curtail smoking The patient's occupation should be considered. Should it involve exposure to excessive amounts of dust or chemical fumes in the atmosphere, a change of occupation may be necessary.

Local Measures.—The nose and throat should be examined for abnormalities which impair the free entry of air and lead to mouth breathing, e.g. deflected septum, polypi, enlarged tonsils and adenoids Chronic infection of the nasal sinuses and tonsils, if present, should receive attention, since this may cause a lowering of resistance to the viruses of the common cold and influenza

Practical experience does not encourage the wearing of masks by healthy people as a safeguard against infection. A mask is more likely to be effective in preventing the spread of infection if worn by persons actually suffering from the disease

Spraying the nose and throat with mild antiseptics, though commonly used as a preventive measure, is probably of no value; nor do we recommend the use of penicillin and sulphathiazole snuffs nor penicillin sprays or lozenges in the prophylaxis of coryza or influenza

Diet and Tonics.—In poorly nourished or debilitated patients, dietetic measures are important in improving the general health It is seldom that a diet is deficient in a quantitative sense, since calories can be purchased cheaply in the form of carbohydrates such as bread and potatoes. The qualitative deficiencies present in the diet of the poorer classes are mainly in animal proteins, minerals and vitamins. This can very easily be corrected by the

who develop infections of the respiratory tract, and fat people sometimes take diets that are deficient in animal protein, vitamins and minerals. Accordingly,

disease of the lungs the effect of this impairment of function may be quite negligible, as such persons possess more than adequate reserves of ventilatory function. In middle-aged and elderly persons, whose reserves of function are diminished by the ageing processes in the lungs and chest wall, and even more

so in patients with organic disease in the lungs, faults in posture and in the mechanics of breathing may be responsible for significant respiratory disability. Whether these faults actually predispose to respiratory infection or to any other type of pulmonary disease is perhaps doubtful, but their correction (see p. 774) is clearly important for maintaining pulmonary function at its highest possible level both in health and disease.

Vaccine Therapy.—Now that it has been established that the common cold is due to a virus, the claims made for bacterial vaccines in the prophylaxis of [illegible]

both the common cold and chronic bronchitis, but proof of such an effect is lacking and there are few authorities who would not agree with the view that the vaccines at present available are of little or no value in the prophylaxis of respiratory infection.

ACUTE CORYZA

(*Acute rhinitis, cold in the head*)

Definition: A catarrhal inflammation of the nasopharynx due to a virus; a secondary infection with pyogenic organisms usually follows.

Treatment will be considered under two heads: (1) measures to abort the infe[illegible]tion, [illegible] there is onl[illegible]metimes possible to abort the incipient coryza by one or more of the following measures

The patient should take a hot bath, followed by a hot drink of lemon or black-currant juice sweetened with sugar, to which 1 oz. of whisky may be added should the patient desire it. Aspirin, 0 3 to 0 6 g (5 to 10 gr.), and the same quantity of Dover's powder (containing opium and ipecacuanha) will secure a good night's rest

To shrink the congested nasal mucous membrane, a 1 per cent. solution of ephedrine in saline may be sprayed into the nose through an atomizer or 1 to 2 drops can be run into the nose by means of a pipette Amphetamine and other local vasoconstrictors, since they temporarily shrink swollen mucous membranes and thereby clear the exits of the air sinuses, are held to be of value in reducing the risks of sinusitis Though the claims made by the manufacturers are often exaggerated, there is little doubt that a temporary symptomatic improvement does occur. *It is necessary, however, to advise against the excessive use of* preparations of this type. If used too frequently, the secondary reaction which follows the vasoconstriction may cause a turgescence of the mucous membranes greater than before, and may lead to an increase of inflammation or even necrosis of the epithelium Accordingly, local vasoconstriction should not be attempted more than three or four times in the twenty-four hours, except in cases of acute infection where the instillation of 1 per cent. ephedrine in saline may be required more frequently in order to prevent obstruction and infection of the nasal sinuses. This preparation has no *deleterious effects on ciliated mucous* membrane [illegible]

Treatment of the Established Condition.—If the measures already

rapid cure is to remain indoors in an even temperature in a well-ventilated but warm room for twenty-four to forty-eight hours. By this means the liability to serious sequelæ from extension of the inflammation to the nasal sinuses and the bronchi is reduced to a minimum.

Patients with acute coryza should realize that they are suffering from an infectious disease which they may pass on to others with results which may be serious. Hence they have a moral obligation to isolate themselves during the acute infective stage, i.e. during the first twenty-four to forty-eight hours.

It is a time-honoured custom to start the treatment of any acute disease with a purge. Since this question will arise in all the acute respiratory diseases, we propose to discuss it fully now in order to save repetition.

Our own feeling is that the routine administration of calomel or castor oil at the beginning of an illness is to be deprecated, since purging is invariably followed by an upset of the normal rhythm of evacuation, and if carried too far has a debilitating effect. Accordingly, if the patient has had a regular daily evacuation of the bowels up to the onset of the illness, we do not advise the administration of an initial purge. If, however, the patient has been con-

dose will ensure a satisfactory evacuation. Should constipation persist, it is better to rely on small doses of a mild laxative such as senna or cascara at night, followed next morning by an enema. A single evacuation from an enema is less exhausting to a debilitated patient than a series of watery motions resulting from a purgative.

Since acute coryza in the vast majority of cases is a self-limiting disease of short duration, no question arises of supplying a diet which will meet the maintenance caloric requirements. A light, easily digested diet, of the type used in fevers (see p. 3), whose constituents should, within reason, meet with the patient's approval, is all that is required.

Drugs.—Provided there are no complications, the only drugs required are

indicated in uncomplicated coryza.

Local Treatment.—In our experience the most suitable form of local treatment is the instillation of 1 per cent. ephedrine solution in saline. The inhalation

Cough Mixtures.—It is traditional for the doctor to prescribe a cough mixture for his patients suffering from acute and chronic bronchitis. Since widely differing opinions are held about the value of cough mixtures, we propose to discuss the matter in some detail.

Cough mixtures can be divided into two main groups. A sedative cough linctus is prescribed for checking a painful non-productive cough which is exhausting the patient and preventing him from resting or sleeping. The two most suitable preparations are syrup of codeine phosphate, 4 to 12 ml. (60 to 160 min.) and linctus methadone N.F (Linctus Physeptone, Burroughs Wellcome & Co.), 4 to 8 ml. (60 to 120 min.). The latter is the more effective.

Expectorant cough mixtures are employed for liquefying viscid bronchial secretions, increasing their flow and facilitating their expulsion. For these purposes the following drugs are frequently prescribed singly or in combination —ipecacuanha, squill, senega, ammonium carbonate, ammonium chloride and potassium iodide

While universal agreement exists in regard to the value of sedative cough mixtures in suitable cases, the same cannot be said about expectorant cough mixtures. Accordingly, it would appear desirable to consider briefly the evidence on which the claims to their therapeutic value are based. The evidence obtained from experiments on animals such as the rabbit, guinea-pig and cat is conflicting, some workers claiming that the output of bronchial secretion is increased by expectorant drugs, while others state the results are negative. Even if the positive results claimed to occur are accepted, their clinical implications must be interpreted with great caution, because the dosage used in animal experiments was relatively enormous, and if given to man in equivalent dosage based on body-weight would have certainly produced vomiting and possibly serious or even fatal poisoning. It is thus apparent that the clinical value of expectorants can be assessed only by trial in patients This is notoriously difficult because of the tendency to improvement which occurs spontaneously within a few days in most cases of acute bronchial catarrh and of the fluctuation in the amount of

it ... u
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pr... t-
taneous variations similar to those seen in the control periods. Alstead states that the opinions of patients as to the value of various cough mixtures was found to be wholly unreliable, judging by their assessments of inert substances such as cochineal in water.

The fact that an emetic dose of ipecacuanha taken on a fasting stomach reflexly causes an increase of bronchial secretion, which is removed together with the gastric contents by the violent muscular efforts accompanying vomiting, does not justify the assumption that a small subemetic dose taken on a full stomach will reflexly cause an increase in bronchial secretion. Similarly, the fact that potassium iodide may induce coryza and increased bronchial secretion

in people who have an idiosyncrasy to the drug does not prove the value of iodides as expectorants. Nor does the finding of traces of potassium iodide in the sputum within a few minutes of its administration necessarily indicate its

It will be generally agreed by the unbiassed observer that the therapeutic

practice are of any therapeutic value, many doctors will wish to adhere to traditional methods of treatment. It is sometimes argued that patients usually expect a bottle of medicine, and that the psychological benefits are undoubted even if the pharmacological effects are dubious. Cough mixtures containing drugs in pharmacopœial doses are indeed harmless to the patient but may be dangerous to the doctor prescribing them, since by attributing to his skilful prescribing results which may have been otherwise produced, he blunts that

form of treatment

The beneficial effects of hot drinks in loosening secretions are not fully realized. They are probably more valuable than cough mixtures. The action may well be partly reflex in character, arising from thermal stimulation of the gastric mucosa. In addition, fluids relieve the state of dehydration—a condition which is likely to develop overnight in febrile patients, in these circumstances too, when the combined effects of dehydration, mouth breathing and trauma to the fauces causes irritability of the pharynx, copious hot drinks are a very valuable form of treatment.

Antispasmodic Drugs.—These may be required for the relief of bronchospasm. Adrenaline subcutaneously and aminophylline intravenously are the drugs of choice when the spasm is *intense*, lesser degrees of spasm may respond to adrenaline or isoprenaline by inhalation, to isoprenaline sublingually or to ephedrine by mouth The oral administration of aminophylline may be effective, but the large doses required are seldom tolerated. The dosage of these drugs is given on p. 684 It is doubtful if the so-called antispasmodic cough mixtures containing lobelia, stramonium or belladonna are of any value in

that the patient should have a holiday of at least one or two weeks before returning to work. Exercise in the fresh air and good nourishing food are far more valuable than ultra-violet radiation, cod-liver oil or vitamin preparations

CHRONIC BRONCHITIS

Chronic bronchitis is the name given to the clinical syndrome which may result from the long-continued action of various types of irritant on the bronchial mucosa.

The ætiological factors of importance include (1) respiratory infection; (2) dust, smoke and fumes, which may occur as specific occupational hazards or as part of the atmospheric pollution in industrial areas; (3) tobacco smoke; and (4) a damp, cold and foggy climate. All these factors also operate in maintaining and aggravating the established condition. It is possible that a constitutional predisposition to chronic bronchitis may be inherited.

The earliest pathological changes are found in the bronchi where there is gross overaction of the mucus-secreting glands; in advanced cases the bronchioles and the associated pulmonary lobules are damaged by what is virtually a low-grade suppurative broncho-pneumonia.

The factors causing breathlessness and wheeze are bronchospasm and partial bronchial obstruction by mucosal œdema or by mucus and pus; in many cases, emphysema leads to increasing dyspnœa on exertion.

Since we are unable to reverse the bronchial and pulmonary changes in chronic bronchitis, treatment is essentially palliative. Nevertheless, a great deal can be done by conscientious medical care to reduce the severity of the symptoms and possibly even to limit the rate of progression of the disease.

Before treatment is started it is a wise precaution to examine the chest radiologically in all patients believed to be suffering from chronic bronchitis to exclude diseases such as pulmonary tuberculosis, bronchiectasis and bronchogenic carcinoma.

The therapeutic approach to chronic bronchitis is along four lines:

1. The avoidance, as far as possible, of the continued inhalation of irritant substances.
2. The prevention and treatment of respiratory infection.
3. The treatment of cough and bronchospasm.
4. General advice about the modifications required in the patient's way of life.

Avoidance of the Inhalation of Irritant Substances.—Heavy pollution of the atmosphere in the industrial areas of Great Britain by smoke, dust and irritant gases is a potent cause of chronic bronchitis and its acute exacerbations. It is thus logical to advise such patients to live in some other place where fog and smoke are negligible. Unfortunately such advice is usually socially or economically unacceptable. The patient's occupation, however, should be considered, since a dusty or smoke-laden atmosphere may have an adverse effect on the bronchitis The remedy may lie in the use of a respirator or in better ventilation in the factory or workshop, but probably nothing will be really effective short of a complete change of occupation.

We are satisfied that smoking is a factor of importance in maintaining and aggravating chronic bronchitis, and there is no doubt that the inhalation of cigarette smoke is particularly harmful. Usually patients are loath to give up tobacco, but we have seen so much benefit arising in those who have stopped smoking that we strongly advise all bronchitics to do so.

The Prevention and Treatment of Respiratory Infection.—The prevention of respiratory infection is dealt with on p. 648.

Patients with chronic bronchitis are extremely prone to develop acute pyogenic respiratory infections, which may take the form of acute bronchitis or sometimes of a low-grade broncho-pneumonia. The most reliable indication of the presence of significant respiratory infection is the expectoration of purulent or mucopurulent sputum Acute infection not only aggravates the symptoms but may be expected to increase whatever permanent pulmonary damage may have already been sustained, it must always be treated promptly and effectively. The most common pathogenic organisms found in the purulent sputum of chronic bronchitis are the pneumococcus and *Hæmophilus influenza*; they may occur singly or together. Penicillin, which should be given intramuscularly in a dose of 500,000 units twice daily either of the crystalline preparation or of a suitable mixture of the crystalline and procaine preparations, is effective against the pneumococcus but of little or no value against *H. influenza*. When penicillin fails to render the sputum mucoid within four or five days it can usually be assumed, even in the absence of bacteriological proof, that *H. influenza* is the predominant organism. Faced with this situation, the physician has the choice of three other drugs, all effective against *H influenza*: (*a*) streptomycin, (*b*)

the commercially available mixture of penicillin and streptomycin (e g. Crystamycin) provided the doses recommended above are adhered to.

Infection is liable to recur after antibiotic therapy is discontinued, but sometimes quite long remissions are obtained, especially during the summer months. Where recurrences of infection are so frequent or so serious as to incapacitate the patient or to endanger his life, attempts have been made to control it with continuous chemotherapy given on a long-term basis Oxytetracycline and tetracycline have been used for this purpose, but in our view the dangers of this type of therapy outweigh the potential benefits for the following reasons:

and lungs.

In all cases the nose and throat should be carefully examined for abnormalities which by obstructing the airway encourage mouth breathing, and also for infected tonsils or nasal sinuses whose secretions may be draining into the bronchi, particularly during the night.

Treatment of Cough and Bronchospasm.—There are few chronic

N.F.) in hot water, taken if necessary with an antispasmodic drug such as ephedrine or isoprenaline. This should be followed by a purposeful bout of coughing and expectoration. If this simple ritual is followed each morning it may spare the patient many paroxysms of tiresome unproductive coughing later in the day and keep his breathlessness and wheeze down to a minimum. If there is a large quantity of purulent sputum, postural coughing should be given

a trial (p. 676). Our views or
already been stated (p. 654).
sputum may call for chemot
when the sputum is mucoid. Nocturnal cough, if it disturbs sleep, should be suppressed by a sedative cough linctus containing methadone or codeine.

Bronchospasm may on occasions be so severe as to warrant the use of cortisone or corticotrophin, but usually an antispasmodic drug such as adrenaline, isoprenaline, aminophylline or ephedrine (p. 684) is sufficient to reduce it to a tolerable level In general, the antispasmodic drugs as well as cortisone and corticotrophin are less effective in what might be termed asthmatic bronchitis than in true bronchial asthma. If the sputum is purulent, control of the infection by chemotherapy may help to relieve asthmatic symptoms and this should always be attempted.

General Measures.—Diet must be adjusted to the needs of the individual. In the debilitated person a high calorie diet with plenty of milk should be advised, but the fat patient needs the weight-reducing measures outlined on p. 324 Regular exercises in the fresh air should be prescribed—always within the limits of the patient's tolerance—but during foggy and damp weather he should stay indoors. General advice should be given about the harmful effects of wearing excessively heavy and thick clothing. Boots and shoes must be strong enough to keep the feet warm and dry.

It is scarcely necessary to draw attention to the harmful effects of excessive quantities of alcohol on the general health; but little harm will be done if it is taken in moderate amounts, and in older patients the sedative and hypnotic effect of alcohol can be used to advantage.

Postural and breathing exercises (p. 774) are valuable in all cases as a means of maintaining efficient pulmonary ventilation and are particularly useful in children and adolescents to prevent chest deformity.

EMPHYSEMA

Diffuse pulmonary emphysema is a common accompaniment of chronic ... respiratory ... apparent ... lar walls, which are its two chief histological features, are, once established, virtually irreversible, although the rate of progress of the disease varies considerably from case to case. Eventually a stage is reached where there is a serious reduction in the efficiency of pulmonary ventilation and of the distribution of inspired air to the alveoli and of pulmonary arterial blood to the related capillaries. These disturbances give rise to exertional dyspnœa and, later, to anoxæmia, pulmonary hypertension and congestive cardiac failure.

In those cases in which the emphysema is secondary to chronic bronchitis or bronchial asthma, appropriate treatment for the primary condition should be instituted (pp. 656, 683). If successful, this will not only provide some measure of symptomatic relief but may also limit the rate of progress of the emphysema. Unfortunately, with the methods at present available for the treatment of chronic bronchitis in particular, this expectation is seldom realized.

The treatment of acute respiratory infection has, however, a more specific part to play in the management of emphysema. In the more advanced cases

congestive cardiac failure is precipitated by acute bronchial or pulmonary infection which, by a mechanism as yet incompletely understood, raises the [illegible]

[illegible]

broncho-pulmonary structure and function.

Symptomatic Treatment.—The symptoms of established emphysema which demand relief are exertional dyspnœa and, at a later stage, those caused by arterial anoxæmia and the retention of carbon dioxide in the blood In emphysema pulmonary ventilation is mechanically inefficient, too little use is made of the diaphragm, and hence the cervical and intercostal muscles are pressed into service—even though these accessory muscles function by the relatively cumbersome method of lifting the whole thoracic cage. Breathing exercises designed to correct these faulty movements are, in our view, of considerable value (see p. 774) Where bronchial spasm is present, it should be promptly treated by means of spasmolytic drugs

A tight abdominal binder or the induction of an artificial pneumoperitoneum is sometimes recommended for the relief of dyspnœa The same principle governs both procedures, that of raising the diaphragm in order to increase its range of movement and reduce the residual volume of the air in the lungs. In practice neither procedure is of any real value

Anoxæmia and the retention of carbon dioxide in the blood are found in the advanced stages of emphysema and are particularly prone to follow acute episodes of respiratory infection. They are often associated with right-sided heart failure. Oxygen therapy is of little practical value in chronic low-grade anoxæmia, but will provide considerable symptomatic relief when a more severe degree develops In the deeply cyanosed patient, oxygen should always be administered. It must, however, be used with caution in view of the danger of a rise in the carbon dioxide content of the blood which sometimes occurs as a result of pulmonary hypoventilation, when the anoxic stimulus to respiration is abolished by the administration of oxygen The commonest clinical manifestations of carbon dioxide retention, formerly ascribed incorrectly to "oxygen poisoning", are headache, mental confusion, sweating, muscular twitching, drowsiness and coma. The appearance of these symptoms is an urgent indication for stopping oxygen and thereafter giving it intermittently or at a low rate of flow (1 to 3 litres per minute). If a patient remains comatose after the administration of oxygen is stopped, vigorous efforts should immediately be made to increase his pulmonary ventilation by stimulation of the respiratory centre. This may be achieved by the intravenous injection of nikethamide, 10 to 15 ml, and aminophylline 0 5 g, which is often followed by a rapid recovery of consciousness. More elaborate methods of increasing pulmonary ventilation, involving the use of a mechanical respirator or of positive pressure respiration through an endotracheal tube, may have a place in the treatment of carbon [illegible]

of work is damp or dusty, an attempt should be made, with the help of the Ministry of Labour, to find him more suitable employment.

THE PNEUMONIAS

INTRODUCTION AND CLASSIFICATION

Prior to the discovery of anti-pneumococcal serum, sulphonamide drugs and antibiotics, the treatment of pneumonia consisted essentially of good nursing and general symptomatic measures. The pneumonias at that time were classified solely on an anatomical basis (*lobar pneumonia and lobular or broncho-pneumonia*), as classification on a bacteriological basis carried little advantage prior to the discovery of effective bacteriostatic or bacteriolytic drugs There is available at the present time a variety of drugs which are therapeutically *effective* in varying degree against the many pathogenic agents which can cause pneu- [illegible]

[illegible]

satisfactory, since the disease process was often segmental rather than lobar in distribution. Much less common than pneumococcal pneumonias are the specific pneumonias caused by:

(*a*) *Staphylococcus aureus*,
(*b*) *Streptococcus pyogenes* (hæmolytic streptococcus);
(*c*) Friedlander's pneumobacillus (*Klebsiella pneumoniæ*);
(*d*) The tubercle bacillus.

The Specific Virus and Rickettsial Pneumonias.—The following viruses and rickettsiæ are known to produce specific types of pneumonia:

(*a*) psittacosis—ornithosis group of viruses;
(*b*) rickettsia of louse-borne typhus fever,
(*c*) rickettsia of Q fever.

The pneumonotropic virus or viruses responsible for most cases of virus *pneumonia in Great Britain have not* been identified. The influenzal virus is not believed to produce a specific pneumonia. Pneumonia complicating influenza is due to secondary bacterial invasion.

The Aspiration Pneumonias.—The organisms causing this group of pneumonias consist of the commensal organisms of the upper respiratory tract and the mouth, e.g. pneumococci, staphylococci, streptococci, hæmophilus influenzæ and anærobes such as Vincent's spirochætes and fusiform bacilli. Aspiration pneumonias may arise in a variety of ways.

(*a*) The pneumonia may result from a direct extension of infection or the aspiration of infected secretions from the smaller bronchi into the alveoli of the lung The pneumonic process is lobular in distribution and affects *both lungs* simultaneously. This type of pneumonia is generally called *broncho-pneumonia*.

(*b*) The inhalation of blood from the upper respiratory passages, vomitus or

septic material from infected sinuses, teeth and tonsils during sleep or during and after operations in these areas may lead first to absorption collapse of those parts of the lungs supplied by the bronchi in which the aspirated material lodges, and then to aspiration pneumonia. A similar type of pneumonia may result from the aspiration of pus from a pre-existing suppurative lesion in the lung, e.g. bronchiectasis or lung abscess, into a healthy portion of lung.

Important factors which facilitate the production of aspiration pneumonia are inadequate drainage consequent on pre-existing bronchial and pulmonary disease such as bronchial obstruction and pulmonary fibrosis, and lowering of the normal defence mechanisms of the respiratory tract to commensal organisms. Depression of the higher centres of the brain by anæsthesia, drugs or alcohol, and inefficient expectoration due to pain (post-operative or traumatic), debility or immobility, are additional causes of defective drainage which should be remembered Depending on the nature and virulence of the infection and the local and general resistance of the patient, aspiration pneumonia can be of so mild a degree as to be recognizable only by radiological examination of the lungs (*benign aspiration pneumonia*) or so severe as to lead to grave pulmonary suppuration (*acute suppurative pneumonia*). When the suppuration is localized and intense, it results in the development of a *lung abscess*, which can be recognized macroscopically as a lesion which is merely one form of suppurative pneumonia. The absorption collapse which results from obstruction of a bronchus or bronchi by viscid secretion which collects in the bronchial tree during and after an operation and which is not expectorated owing to weakness and post-operative pain, is often followed by so-called *post-operative aspiration pneumonia*. It should be noted, however, that initially at least this condition is due to bronchial obstruction and not to infection. Another member of the group of aspiration pneumonias is called *hypostatic pneumonia*. This form arises from infection by commensal organisms of secretions which have gravitated to the lung bases. It develops especially in elderly, weak, bed-ridden patients who have difficulty in expectoration. The pneumonic process resulting is often relatively mild, but is sufficient to cause death in patients enfeebled by old age or disease.

The treatment of the pneumonias will be dealt with under two main headings.

(1) General measures and symptomatic treatment which are applicable to all forms of pneumonia, and

(2) Specific therapy with sulphonamide drugs and antibiotics which will vary in the different types of pneumonia

GENERAL MEASURES

Since the advent of sulphonamides, penicillin and other antibiotics, many cases of pneumonia may be adequately treated in their own homes, but if the home conditions are poor or overcrowded, admission to hospital should be recommended

If it is decided to treat the patient at home he should be nursed in a warm room with plenty of fresh air at a temperature around 65° F. (18 3° C) Since the illness is usually more serious and more prolonged in elderly patients it is essential to conserve their strength by relieving them of every effort. Skilled nursing, accordingly, is always necessary

The patient should be permitted to assume the position in bed which he finds most comfortable. In general, this is the inclined position, the patient's back

being supported by pillows or a bed-rest. In old and debilitated persons the nurse should alter the patient's position in bed from time to time as by doing so, the liability to hypostatic congestion is reduced to a minimum. The danger of venous thrombosis in the legs should be remembered and measures undertaken for its prevention (see p. 92) Active and passive movements of the lower limbs and deep-breathing exercises should be regularly carried out as soon as the patient's condition permits.

The measures relating to clothing and diet are described in the section on acute bronchitis (p. 652).

SYMPTOMATIC TREATMENT

Pain in the Chest.—With modern chemotherapy, the duration of pain is generally so short that simple measures, e g. a hot-water bottle and a mild analgesic such as compound tablets of codeine, are almost always adequate. Severe pain leads to much distress, restlessness and insomnia, and here pethidine, 50 to 100 mg, or methadone, 5 to 10 mg, by mouth or preferably by intramuscular *injection will be indicated. Morphine is of great value in obtaining* some hours of rest and sleep, and we use it if necessary in doses of 10 mg. ($\frac{1}{6}$ gr.) subcutaneously in the evening, repeating the dose if required in two hours.

Insomnia and Restlessness.—*If the patient is in a weak, toxic condition,* special management may be needed to ensure sufficient sleep Before resorting to hypnotics, his nursing care should receive attention. Sponging with tepid water, placing the patient in a comfortable position, rearranging the bedclothes, getting him to pass urine and giving aspirin and a hot drink, with or without the addition of whisky, are simple measures which are often effective.

A distressing painful cough calls for the prescription of a sedative linctus (p. 654). When insomnia is due to the restlessness caused by fever and

a full dose of 2 g. (30 gr.)

. (about 22 gr.) may suffice

ıl, one of the barbiturates

may be tried, 0·2 g (3 gr.) of butobarbitone, which is a medium-acting barbiturate, or 0·2 g (3 gr.) of quinalbarbitone, which has a short action. It should be remembered that the use of barbiturates in the elderly may produce mental confusion and restlessness Paraldehyde, 4 to 8 ml. (60 to 120 min.) by

indications to the use of these drugs already stated.

Delirium.—A mild degree of delirium is frequently present in pneumonia—the patient suffers from hallucinations and mild confusion. Marked delirium

is one of the most serious prognostic signs because it indicates intense toxæmia and anoxæmia. Treatment of these severe cases is unsatisfactory as the amount of sedative required to control the delirium may cause death from depression of the respiratory centre. Oxygen is obviously indicated, although the mask or nasal catheter or even the oxygen tent are often badly tolerated. The patient must be restrained, if necessary by strapping the limbs to the bed. In general, however, reliance has to be placed on hypnotics despite their danger. Morphine is contra-indicated because of the anoxæmia. The effects of barbiturates in these circumstances are unpredictable; they may fail, or they may aggravate the mental confusion. Chloral hydrate may be a very valuable drug on these occasions, but only if the patient will swallow a full dose of 2 g (30 gr.)—this must be dissolved in not less than 4 oz water (suitably flavoured with syrup of ginger) in order to reduce the risk of vomiting. In general, paraldehyde is the drug of choice. Oral or rectal administration is seldom tolerated by confused or delirious patients; 5 ml should therefore be injected intramuscularly and a further dose of 5 ml may be given after one hour if necessary. If the patient is an alcoholic, paraldehyde will probably prove useless, because of the phenomenon of cross-tolerance. On the assumption that oral medication is [illegible] that paraldehyde has failed, an injection of hyo[illegible] if possible, 0.3 mg ([illegible] gr.) [illegible] intramuscularly, [illegible] but this takes long [illegible]

Cyanosis.—As [illegible] which is a frequent [illegible] in all cases, and [illegible] of death in pneumonia, [illegible] reliable clinical index of anoxæmia, appears. If severe emphysema is present, oxygen therapy (see p. 880) must be looked for carefully should be observed. [illegible] must be started immediately it [illegible] the precautions mentioned on p. 882

Circulatory Failure.—Circulatory failure in pneumonia may present in two forms which not uncommonly coexist.

1. Cardiac failure.
2. Peripheral circulatory failure.

Cardiac Failure.—Where the circulatory failure is primarily central, its two most common causes are (*a*) auricular fibrillation and (*b*) pulmonary heart disease (cor pulmonale).

Auricular fibrillation may develop in the course of pneumonia, especially in middle-aged and elderly patients. If it is allowed to persist for more than forty-eight to seventy-two hours with a rapid ventricular rate, congestive cardiac failure is likely to supervene. A single intravenous injection of digoxin, 1 mg, sometimes restores normal rhythm. If it fails to do so, the patient should be fully digitalized by the oral route (p. 528); this will reduce the ventricular rate and prevent the appearance of frank congestive failure, or control it if it has already appeared. Normal rhythm frequently returns during the course of treatment, but it is always difficult to be certain whether or not digitalis should be given the credit for this. If ischæmic heart disease is present, the arrhythmia may persist and a maintenance dose of digitalis has then to be continued indefinitely.

Other measures such as mersalyl and a low salt diet will be required when frank congestive heart failure with peripheral and pulmonary œdema supervene.

If the pneumonia occurs in a patient with chronic bronchitis and severe

equally satisfactory in the average case—100,000 units six-hourly or 500,000 units twelve-hourly. Injections of 500,000 units of penicillin twice daily are as effective as six-hourly dosage in pneumococcal pneumonia, and this suggests that it is not essential to maintain *continuously* the theoretical "therapeutic concentration" in the blood; the amount of penicillin in the infected tissues is

until the temperature has been normal for at least three days.

Penicillin by inhalation is not recommended, since only low concentrations of penicillin are obtained in the blood by this method of administration.

Penethamate hydroiodide (Estopen), when given intramuscularly, is concentrated in the lungs and excreted in the sputum in relatively high concentration. The claims that this preparation is superior to ordinary penicillin in the treatment of pneumonia, however, have not been confirmed; moreover,

n. The
y four or
six hours until crisis or lysis has occurred and continued thereafter for at least three days.

If there has been no response within forty-eight hours of the beginning of treatment with penicillin and/or sulphonamide, the practitioner should (*a*) review the diagnosis of pneumonia and consider the possibilities of pulmonary abscess, empyema, pleural effusion, atelectasis due to bronchial carcinoma, pulmonary infarction or tuberculosis, and (*b*) consider the possibility that the pneumonia is caused by organisms insensitive to penicillin and sulphonamide. If a sample of sputum has been sent to the bacteriological laboratory for culture and sensitivity tests on the first day of the illness, a report should now be available which will be of great value in determining the correct form of specific therapy to be adopted. If no such information is available, an antibiotic with a wide therapeutic range (one of the tetracycline group of drugs or chloramphenicol)

either to a
ılood-borne
infection from a lesion at a distance, e.g osteomyelitis. It is usually a very *serious illness*. Specific treatment consists of the administration of crystalline penicillin in large doses, e g. 1 mega unit followed by 0·5 mega unit every six
treatment with the appro-
ıtituted at once
l of seven to ten
days.

Streptococcal Pneumonia.—*Pneumonia due to hæmolytic streptococci is*
of the throat.
onia. The
factory and
eumococcal
pneumonia.

Pneumonia due to Friedländer's Pneumobacillus.—This form of pneumonia is fortunately rare. It causes a very serious illness which often results in permanent damage to the affected lung. A massive lobar consolidation, often affecting the upper lobe, occurs. The sulphonamide drugs and penicillin are relatively ineffective, and the drug of choice is streptomycin given by intramuscular injection in doses of 1 g six-hourly. This should be continued until the temperature has been normal for three or four days, or for a maximum of seven days. It is important to assess the sensitivity of the bacillus to the various antibiotics at the earliest possible stage as some strains are resistant to streptomycin and one of the other drugs may then have to be given.

Tuberculous Pneumonia.—See p. 122

Virus and Rickettsial Pneumonias.—In this group of pneumonias fever and constitutional symptoms precede the respiratory symptoms for some days. The signs are frequently minimal on physical examination although easily seen radiologically. The illness is rarely fatal and usually spontaneous recovery takes place within ten days. The name "primary atypical pneumonia" is sometimes applied to the pneumonias resulting from unidentified types of virus, but this name has little to recommend it and should be discarded. One of the tetracycline group of drugs or chloramphenicol should be used in severe cases of virus pneumonia, although their efficacy is doubtful

The Aspiration Pneumonias.—The great danger of suppuration and permanent damage to the structure of the lung which occurs in this group of pneumonias clearly indicates the need for taking all possible measures to prevent their development and for their early diagnosis and effective treatment As already mentioned, aspiration pneumonia may be so mild as to be scarcely recognizable or so severe as to cause a grave or even fatal illness.

Prophylaxis.—The danger of inhaling infected material from the sinuses, tonsils and teeth during sleep or following operations in these regions should be remembered as a cause of aspiration pneumonia and the necessary precautions taken to eliminate this risk After operations requiring general anæsthesia, morphine should be administered cautiously in view of its depression of the cough reflex The patient should be encouraged to cough up secretions and thus avoid bronchial obstruction. Should this be insufficient to clear the bronchi, bronchoscopic aspiration should be undertaken. Postural coughing should be carried out at regular intervals by patients with bronchiectasis or lung abscess, as this is a valuable means of preventing the development of the type of aspiration pneumonia which arises from the transference of infected material from a diseased to a healthy portion of lung

Treatment—The drug of choice in all forms of aspiration pneumonia is penicillin, which should be given in high dosage (500,000 units six-hourly of the crystalline preparation) as the organisms responsible for the infection are often less sensitive than pneumococci The choice of antibiotic in these cases must always be reviewed in the light of sensitivity tests, but with the reservations mentioned on p. 666. The usual measures to promote expectoration should be instituted, such as hot alkaline drinks and postural drainage. Bronchodilator drugs are indicated if bronchial spasm is present. Antibiotic treatment must often be more prolonged than for pneumococcal pneumonia and may have to be continued for two or three weeks, or even longer when there is evidence of persisting pulmonary suppuration

CONVALESCENCE

After an acute attack of pneumonia, it is most desirable that the patient should have a holiday of at least a fortnight—and preferably a month—before he

illness, it is usually possible to make arrangements in good time for a holiday in the country or at the seaside. Occasionally the help of the hospital almoner will be required. Care should be taken not to send the patient to a holiday resort at

undertaken for five minutes several times a day. While no artificial measures

winter.

Delayed Resolution.—Resolution may be delayed because of structural disease (neoplasm, bronchiectasis, fibrosis) which was present before the onset of pneumonia. A careful investigation to eliminate such a cause must be undertaken and appropriate treatment instituted. In all other cases of delayed resolution postural coughing followed by breathing exercises should be undertaken several times a day and a prolonged convalescence should be advised.

When the delay in resolution is due to plugging of the smaller bronchioles

possible to determine the exact site and nature of a bronchial obstruction.

PLEURISY

The symptomatic treatment of pleurisy is discussed on p 662. Otherwise its treatment is that of the underlying disease.

EMPYEMA

ACUTE EMPYEMA

type of pneumonia. Before the intro-

decreased considerably. Although pneumococcal pneumonia still accounts for many cases, another important cause of empyema is non-specific pulmonary suppuration due to the aspiration of infective material from the upper respiratory tract, or occurring as a complication of bronchiectasis or of bronchial obstruction by a carcinoma. *Staphylococcal* pneumonia is a not uncommon cause of

empyema, especially in children. Rarely, an empyema results from the extension of an infective process in the chest wall, the mediastinum or the abdomen.

The diagnosis of empyema is established by the aspiration of pus from the pleural space. Before attempting aspiration the position of the empyema should be localized accurately by means of postero-anterior and lateral radiographs. Since the pus is sometimes thick, a wide-bore needle should always be used.

In contrast with a serous pleural effusion the absorption of pus from an empyema does not occur spontaneously even if the pus has become sterile following treatment with penicillin. On the contrary, with the passage of time the pus tends to become progressively thicker and the walls of the empyema cavity more rigid.

It is thus clear that the primary objective in the treatment of acute empyema must be the evacuation of all the pus at the earliest possible stage and the prevention of its reaccumulation. This can be achieved in three ways:

(a) By repeated aspiration of the pus with a two-way syringe and needle, while an attempt is made to control the pleural infection by the systemic and intrapleural administration of a suitable antibiotic.
(b) By continuous drainage of the empyema at its most dependent point by means of a rubber tube inserted either through an intercostal space or following rib resection.
(c) By resection of the empyema *in toto*.

Conservative Treatment.—Conservative treatment is indicated only when the empyema is recognized at an early stage, i.e. when the pus is thin and easy to aspirate and when rapid and complete re-expansion of the lung is not prevented by thickening of the visceral pleura. These indications must be strictly observed as there is otherwise a considerable risk of the empyema becoming chronic and consequently more difficult to treat surgically.

Conservative treatment is carried out in the following manner.

Aspiration.—As much pus as can be obtained is aspirated daily or on alternate days for the first week and at progressively longer intervals thereafter. Frequent radiological examination is essential to ensure that re-expansion of the lung is proceeding satisfactorily.

Antibiotics.—Most of the bacteria responsible for acute empyema are sensitive to penicillin and, pending bacteriological confirmation, treatment with penicillin should be instituted on the assumption that the organisms are penicillin-sensitive. Provided that the condition is not tuberculous, this assumption is also justifiable if pus obtained from a patient already treated with penicillin is found to be sterile.

Crystalline penicillin is injected intrapleurally after each aspiration in a dosage of at least 500,000 units dissolved in 5 ml of sterile water. This alone will generally produce a therapeutic blood concentration, but it is usual to raise it still further by the intramuscular injection of 250,000 units of penicillin every six hours.

In the event of penicillin-resistant organisms being isolated from the pus, an antibiotic to which they are sensitive should, if possible, be substituted for penicillin. Unfortunately, with the exception of streptomycin, preparations of the other antibiotics suitable for intrapleural instillation are not yet available. Unless there is a prompt response to repeated aspiration combined with the

systemic administration of the appropriate antibiotic, conservative treatment should be abandoned and the case referred to a thoracic surgeon. Indeed, in

The *intrapleural injection* of two fibrinolytic enzymes, streptokinase and streptodornase, to liquefy the pus is not now recommended as it is successful only in a minority of cases and is liable to cause unpleasant reactions.

The success or failure of conservative treatment in acute empyema is usually apparent within seven to ten days. *It is seldom profitable to continue such* management for longer unless substantial progress has been made, and it may prove necessary to abandon it at an earlier stage if the pus becomes thick and difficult to aspirate. A successful outcome can be assumed when, following a steady reduction in the amount of pus obtained at successive aspirations, a stage is reached at which none at all can be obtained. At the same time the patient

surgeon, who will decide whether to resect or drain the infected pleural sac.

CHRONIC EMPYEMA

The development of a chronic empyema has two main causes:

1. Delayed or inefficient treatment of an acute empyema, resulting in the formation of a rigid cortex of organizing fibrin on the surface of the lung, which is thus prevented from re-expanding.

2. *Diseases in the underlying lung, such as tuberculosis, bronchiectasis* or bronchial carcinoma, which not only facilitate the initial pleural infection but also prevent its healing by rendering the lung incapable of full re-expansion.

resection of the empyema *in toto*.

In the second group treatment depends on the nature of the underlying disease. When bronchiectasis or a bronchial carcinoma is present, the infected pleural sac is resected along with the primary lesion if practicable; otherwise it is drained. When the chronic empyema is due to tuberculous infection of the pleura secondary to pulmonary disease an attempt should first be made to control the infection by repeated aspiration of the pus and by the intrapleural administration of streptomycin combined with systemic *anti-tuberculous* Often it will be possible to secure obliteration of the pleural

form of surgery is required.
along with the diseased lung,
not be undertaken until the
pulmonary disease has been at least partially controlled by specific chemotherapy.

Spontaneous pneumothorax is due to a breach in the continuity of the lung surface, allowing the escape of air into the pleural space. This commonly results from the rupture of an emphysematous bulla or the tearing of a pleural adhesion at its pulmonary attachment, or more rarely from the ulceration of a superficial tuberculous focus or pulmonary abscess.

If there is a large broncho-pleural fistula, e g following the rupture of a tuberculous cavity or pulmonary abscess, pleural infection almost invariably supervenes, with the production of a pyopneumothorax. The treatment of tuberculous pyopneumothorax is described on p 138 and that of non-tuberculous cases on p. 668.

In most instances, however, the pneumothorax is of the so-called benign variety due to the rupture of a subpleural emphysematous bulla The fistula is small and usually closes almost immediately, the air is gradually absorbed, the collapsed lung re-expands and the pleural space never becomes infected Occasionally the fistula persists as a small valvular opening, in which case the intrapleural pressure rises above atmospheric level, the lung collapses completely and ventilation of the opposite lung is impaired by mediastinal displacement. The state of " tension pneumothorax " which results may, if untreated, prove fatal.

The first decision to be made after the diagnosis is reached is whether or not emergency treatment is required for the relief of intrapleural tension. Urgent dyspnœa, especially if accompanied by cyanosis, suggests that a tension pneumothorax is present and calls for the immediate insertion of a wide-bore needle into the pleural space (p 873) The needle should be firmly fixed in position by means of a flat cork and adhesive tape, and connected to a length of rubber ubing, the end of which is placed in an unstoppered bottle on the floor conuning sufficient water to cover completely the exit of the tube. This improvised water-seal " drainage system allows air to escape from but not to re-enter the uest.

The patient should be given an injection of morphine to relieve pain and apprehension. As soon as the severe breathlessness has subsided he should be conveyed to hospital with the needle *in situ* If necessary, oxygen should be administered on the journey as well as on arrival Radiological examination of the chest should be undertaken immediately to confirm the diagnosis The needle is then replaced by a rubber catheter introduced by means of a trocar and cannula and connected to a water-seal drainage system, to which negative pressure is applied by means of an electric pump Complete re-expansion of the lung is usually obtained within twenty-four hours by this method, which undoubtedly represents an important technical advance in the treatment of tension pneumothorax. Although the fistula generally closes, as soon as the visceral and parietal pleural surfaces come into contact, it is advisable to keep the tube in place for five to seven days to ensure that the fistula seals off completely and to encourage the formation of pleural adhesions, which may prevent further episodes If the pneumothorax is accompanied by a pleural effusion, the fluid can either be drained through the catheter by suitable posturing or aspirated with a syringe and needle Penicillin in prophylactic dosage should be given intramuscularly as long as the tube remains in the pleural space.

All other cases of spontaneous pneumothorax fall roughly into two categories:

1. The pneumothorax is small and the degree of dyspnœa is no more than slight.
2. The pneumothorax is large and dyspnœa of moderate severity is present.

Cases in the first category require no treatment, but the chest should be examined radiologically at weekly intervals until re-expansion of the lung is complete. The second category should include all cases in which the lung is more than one-third collapsed. Here, several weeks may pass before there is complete absorption of the air. This period can be considerably reduced if the air is removed by the method used for the treatment of tension pneumothorax.

The same general principles apply to the treatment of cases with an active tuberculous lesion in the underlying lung, with one important exception. If a pleural effusion develops, particularly if tubercle bacilli are found in the fluid, re-expansion of the lung must be secured with all possible speed in order to

[illegible]

the presence of a pneumothorax, especially if it is large, may be misleading, as intrapulmonary disease, especially tuberculosis, may be obscured by collapse The examination must therefore be repeated after the lung has re-expanded. If there is any sputum it should be examined repeatedly for tubercle bacilli; and the erythrocyte sedimentation rate should be estimated weekly. Thoracoscopy would be expected to provide useful information regarding the cause of the pneumothorax; but in practice the findings seldom help in diagnosis or treatment, and in most cases the examination can safely be omitted.

[illegible] tuberculous lesion is found in the underlying lung, or for that

[illegible]

the lung long after the patient has recovered from a pneumothorax. It is therefore a wise precaution to keep him under observation for six months.

[illegible]

surfaces In our experience the presence of a rubber tube in the pleural space [illegible] suffices to achieve this, but some authorities believe that, in addition, an [illegible] in oil, hypertonic glucose or [illegible] space.

Chronic Spontaneous Pneumothorax.—When a *valvular* fistula persists for months or even years it can often be successfully treated in the same way as a tension pneumothorax. In some cases, however, owing to thickening of the visceral pleura, the lung cannot re-expand and decortication has to be performed.

HÆMOTHORAX

Hæmothorax is by far the most common complication in chest injuries, for it may be associated with any of the various types of injury by blast or crushing in addition to penetrating and perforating wounds.

Blood in the pleural cavity, being in a defibrinated state, remains f over 90 per cent of cases and hence can be aspirated. Treatment by re aspiration will be successful in the majority of cases. If the hæmorrhag been large, a blood transfusion should be started immediately, and as so the patient's general condition permits, the hæmothorax should be compl aspirated. Because extravasated blood is such a favourable medium for bact growth, aspiration should never be delayed. To prevent the development secondary infection, one mega unit of penicillin should be instilled int pleurally after each aspiration. Aspiration may have to be repeated seve times before the reactionary effusion, which invariably follows, ceases reaccumulate. Infection occurs in approximately one-third of cases wit hæmothorax, but even in such circumstances repeated aspirations followed by instillation of penicillin into the pleural cavity may lead to complete cure.

When massive hæmorrhage has occured in the pleural sac and the blood has clotted, thoracotomy is essential, the clot must be removed and decortication of the lung carried out, otherwise it will never re-expand completely. In patients with secondary infection who are too ill to withstand major surgery, preliminary drainage may be required.

In cases complicated by a sucking wound of the chest wall, by a broncho-pleural fistula or by other injuries, special surgical measures will be necessary.

A hæmothorax or a hæmopneumothorax may occur *spontaneously* in the absence of any demonstrable pulmonary lesion. When there is no air in the pleural space, the treatment indicated is that of traumatic hæmothorax. In cases of spontaneous hæmopneumothorax, if only a small amount of air is present, it can be withdrawn by means of an artificial pneumothorax apparatus. When the pneumothorax is large, and particularly if it is under tension, an intercostal tube may have to be inserted and the air removed by suction.

BRONCHIECTASIS

There are wide variations in the clinical picture of bronchiectasis. Occasionally the condition is discovered on routine radiological examination and is symptomless. Other patients may complain only of recurrent cough or of repeated hæmoptysis (bronchiectasis hæmorrhagica sicca) or the classical picture of chronic ill-health; toxæmia, fœtid sputum and clubbing of the fingers may be present. There is, in addition, a large intermediate group in which health is not impaired for many years despite the expectoration of large amounts of sputum. The type, stage and localization of the disease, as well as the age, social circumstances and general health of the patient are factors which must be taken into consideration in determining the most suitable method of treatment.

Prophylaxis

A history of one or more attacks of capillary bronchitis or broncho-pneumonia, usually in childhood, is of such frequent occurrence in bronchiectasis as to suggest that a failure to obtain complete resolution of the inflammatory process is a factor of great ætiological importance. Accordingly, the family doctor should realize the essential need for thorough treatment in the acute stage of broncho-pneumonia by the measures outlined on p. 652. He should also plan the long-term management and convalescence so as to ensure complete resolution. Such measures include a good diet, fresh air, a holiday at a con-

valescent home or elsewhere and breathing exercises carried out regularly two or three times a day. If atelectasis is present, the possibility of bronchial obstruction by tuberculous lymphadenitis should be investigated by bronchoscopy.

The bronchoscope should also be employed for the treatment of collapse due to obstruction of a bronchus by viscid secretion or by a foreign body. The obstruction should be removed as soon as possible because of the liability of the bronchial tree to infection and dilatation.

Since persistent infection of the nasal sinuses and teeth is one of the most important factors in initiating and maintaining infection in the bronchial tree, such conditions should receive prompt and energetic treatment.

Treatment

Since the introduction of antibiotics our views on the prognosis and treatment of bronchiectasis have been substantially modified, mainly because it is now possible in many cases to control the acute exacerbations of infection which have been responsible for most of the mortality and much of the morbidity from the disease. Many patients with advanced bronchiectasis can thus be kept alive and in tolerably good health for many years ; and those with relatively mild or intermittent symptoms are no longer in the same danger of progressing to the advanced stage

For these reasons all cases of bronchiectasis, with the exception of those in which repeated hæmoptysis is the chief symptom, should in the first instance be treated conservatively. Subsequent management will depend partly on the initial clinical and radiological assessment and partly on the response to conservative treatment.

As far as treatment is concerned, it is possible to allocate every case of bronchiectasis to one of three categories. The *first* includes all those cases whose symptoms are adequately controlled by conservative measures, whatever the extent of the disease radiologically. It is seldom justifiable to advise these patients to submit to surgical treatment, but they should always be kept under observation so that if intractable symptoms develop the question of surgical intervention can be reconsidered.

The *second* category comprises those unfortunate patients in whom conservative measures fail and who cannot be offered surgical treatment either because the disease is too widespread or because co-existing severe chronic bronchitis, bronchial asthma or emphysema would gravely increase the hazards of the operation and diminish the prospects of its achieving a satisfactory functional result.

In the *third* category, intermediate between the first two, are those patients whose symptoms are not adequately controlled by conservative measures but in whom the disease is sufficiently limited in extent to permit its complete surgical extirpation without seriously impairing respiratory function.

The greatest care must be taken in selecting cases for surgical treatment *It* is, for example, particularly important to be certain that the symptoms are *in* fact due to bronchiectasis and not to generalized chronic bronchitis, with which it is frequently associated

The surgical treatment of bronchiectasis achieves its greatest success where ...ated by *bronchography*, and ...nchitis or bronchial spasm.

Cases of more extensive bronchiectasis, up to the equivalent of one lung, can of course be successfully dealt with surgically. It must be remembered, however, [illegible]

with age Bronchiectasis should seldom be treated surgically after the age of forty, and then only after conservative treatment has been given a prolonged trial

Repeated severe hæmoptysis constitutes a special indication for surgical treatment. Difficulties may arise when the bronchiectasis is too extensive for total resection and the source of the bleeding cannot be established with sufficient certainty for a local resection to be performed, here, treatment must be expectant until precise information is obtained regarding the site of the bleeding.

The practical aspects of the two types of treatment, conservative and surgical, will now be considered.

Conservative Treatment.—The aims of conservative treatment are threefold: (1) to improve the patient's general health, (2) to control respiratory infection by chemotherapy; and (3) to prevent pus from accumulating in the dilated bronchi by postural drainage.

General Measures.—The measures for raising the general resistance and preventing respiratory infection employed in the treatment of chronic bronchitis (p. 656) are equally applicable in bronchiectasis, since patients suffering from this disease are also subject to frequent episodes of acute respiratory infection. Fresh air and exercise are important, but attention must also be paid to climate, housing, diet, clothing and occupation Iron is indicated if hypochromic anæmia is present (p 404).

[illegible]

exacerbations of infection Their continuous administration on a long-term basis cannot be recommended because of the danger of side-effects and the risk of promoting a drug-resistant bacterial population Infection is, however, often perpetuated by the tendency for pus to accumulate in the dilated bronchi, and if this can be prevented by postural drainage, the control of symptoms seldom presents insuperable difficulties

If the sputum is purulent or fœtid, penicillin (250,000 to 500,000 units six-hourly) and postural drainage should be started simultaneously The penicillin should be continued until the sputum is mucoid in character. If [illegible]

control the acute exacerbations of infection which characteristically recur throughout the course of the disease. They should also be used in circumstances where the *complete* control of infection is essential, for example before and after surgical resection or any other procedure requiring a general anæsthetic, and also prior to bronchography.

Upper respiratory infection, in particular sinusitis, which is a common accompaniment of bronchiectasis, must be dealt with as thoroughly as possible, because, if allowed to persist, it may be an important factor in maintaining infection in the dilated bronchi. The help of an ear, nose and throat specialist must always be obtained in such cases.

Postural Drainage.—The importance of this measure has already been emphasized. Its chief value is in those cases in which one or both lower lobes are involved. The [illegible] the erect position.

lean over the edge o [illegible]

body, which is supported by placing the hands on the floor, so that the bases of the lungs are uppermost. A basin is placed on the floor to catch the expectoration. This posture should be adopted twice daily, on rising in the morning and before retiring at night, for a period of ten to twenty minutes. For elderly or weak patients unable to tolerate this method, raising the foot of the bed as high as the patient will tolerate may be almost as satisfactory. To loosen sputum prior to postural drainage an alkaline mixture followed by a hot drink will be found useful, as also will the inhalation of steam medicated with compound tincture of benzoin (1 teaspoonful to 1 pint of hot water).

Bronchoscopic aspiration of the pus has seldom any advantage over postural drainage. It should not be employed unless there is any clinical or radiological [illegible]

location and extent of the disease, and may vary from resection of a single segment to that of a whole lung or substantial portions of both lungs. With modern operative and anæsthetic techniques the mortality is very small and the results are excellent. Bad results are almost invariably due to faulty selection of cases or to inadequate pre-operative care. The most common mistake is to attempt to treat surgically patients whose bronchiectasis is too extensive or whose respiratory reserve is inadequate. If pre-operative preparation is unsatisfactory, the patient will be liable to post-operative atelectasis or pneumonia through the aspiration of pus into healthy portions of lung. No patient should be submitted to operation unless, by the conservative measures already described, his sputum has been reduced to a minimum. Anæmia must of course always be corrected before operation is undertaken. Patients who have had severe hæmoptysis may require blood transfusion.

PULMONARY ABSCESS

A pulmonary abscess may develop without apparent cause, or it may compli- [illegible]

has been aspiration of infected tissue and blood clot into the bronchi.

The prevention and treatment of post-operative chest complications are of importance in the prophylaxis of pulmonary abscess (see also p. 678). It is not sufficiently realized that if circumstances permit, every patient who is about to undergo a major surgical operation under general anæsthesia should first receive local treatment for sepsis in the mouth and throat. However, the

dental operations.

Before treatment is started, an attempt should be made to discover the cause of the pulmonary abscess. In all cases the sputum must be examined bacteriologically, not only to discover, if possible, the causal organism but also to exclude tuberculous cavitation, which may be mistaken for a pyogenic abscess. Bronchoscopy or bronchography will often be necessary to determine whether the abscess is secondary to bronchial neoplasm or to bronchiectasis, though such investigations may have to be delayed until the acute phase of the illness is past.

The introduction of antibiotics has had an impact on the treatment of pulmonary abscess, more dramatic even than in the case of bronchiectasis.

(1) to improve the patient's general condition and relieve symptoms; (2) to control the infection by chemotherapy, and (3) to keep the abscess cavity or cavities drained by postural coughing

General Symptomatic Measures.—These differ in no essential detail from those recommended for pneumonia (p. 661). Although complete healing of an abscess takes longer than resolution of a pneumococcal pneumonia, the acute phase of the illness is seldom much more protracted now that antibiotics

such as empyema and cerebral abscess, which are now fortunately rare

Chemotherapy.—Until the results of bacteriological examination of the sputum are available, penicillin is the drug of choice, and as many of the organisms are penicillin-sensitive it frequently proves completely effective Its failure is In these circum-
, chloramphenicol
ity tests may help considerably in the selection of the correct drug. However, bacteriologists themselves insist that the results of these tests should be considered in conjunction with the clinical picture. If, for example, a patient is making good progress with penicillin, as shown by his symptoms, the temperature chart and the character of the sputum, this drug should usually be continued even if the bacteriologist reports the predominant organism in the sputum to be penicillin-resistant. The fact that an organism is predominant in the sputum does not necessarily mean that it is responsible for a pulmonary infection. On the other hand

The duration of chemotherapy in pulmonary abscess is important. Because of the rather chronic nature of the lesion treatment must be continued for a period seldom less than six weeks. This advice, however, cannot be followed

with any of the antibiotics except penicillin and possibly the drugs of the tetracycline group, owing to the risk of side-effects.

Postural Drainage.—This should be performed at least thrice daily for thirty minutes until the cavity has ceased to be visible radiographically and the sputum has become mucoid. When the abscess is situated in the upper lobe, postural coughing is carried out, first in the upright position and then in the lateral position with the affected lung uppermost If the abscess is in the right

position or prone, depending on which segment the abscess occupies

Bronchoscopy, although useful as a diagnostic measure, has no part to play in the routine treatment of pulmonary abscess. Unless the patient is very weak, the pus can be expectorated just as efficiently as it can be aspirated through a bronchoscope.

Surgical Treatment.—In the rare instances where conservative treatment fails, the patient may require some form of surgery. At an early stage, if there is no response to chemotherapy, the patient may develop grave toxæmia from an undrained or inadequately drained abscess. In these circumstances external intercostal drainage may be required. Alternatively, the patient may recover fairly well from the acute phase of the illness, but in spite of chemotherapy the abscess cavity may persist or irreversible bronchiectasis may supervene Such sequelæ are best treated by resection of the affected lobe or segment, the results of which are generally satisfactory.

POST-OPERATIVE PULMONARY COMPLICATIONS

The treatment of such complications as bronchitis, pneumonia, abscess of the lung and empyema have been dealt with elsewhere. Subphrenic abscess calls for surgical measures.

ATELECTASIS

Atelectasis is one of the commonest post-operative pulmonary complications. It may be patchy or lobular, or may involve an entire lobe (massive collapse). The onset is usually sudden and occurs within the first twenty-four to forty-eight hours after the operation, particularly an abdominal or thoracic one. The immediate cause of the collapse is obstruction of a bronchus by inspissated mucus or ... from the upper respiratory passages ...
if steps are ...
collapse will be greatly reduced.

Prophylaxis.—*Before Operation.*—When any respiratory infection is present, such as bronchitis or even a cold in the head, the risk of atelectasis is ... be postponed if possible. Heavy ... mplications ... or two weeks prior to operation.

If postponement of the operation is possible, patients with deformities of the chest or faulty methods of breathing should be given a course of breathing exercises.

Secretions are apt to stagnate in the bronchi of elderly patients, particularly if they are obese and flabby. Before operating on these patients measures should be taken to reduce their weight (see p. 324). A pre-operative course of penicillin (see p. 64) combined with postural coughing may be of great advantage in elderly patients with chronic bronchitis.

After Operation—After all major operations the position of the patient should be changed three or four times during the day. The nurse should remove the pillows, place the patient on his side, and instruct him to cough. After abdominal and thoracic operations coughing is painful, but must be encouraged. It will be easier for the patient to cough if the nurse supports the wound firmly with her hand. Constricting bandages around the lower part of the chest and abdomen interfere with expansion of the lower lobes and should never be allowed Flatulent distension has a similar effect and should be corrected [illegible]

be used after operation as it tends to increase the tenacity of the mucus in the [illegible]

Treatment—[illegible] most cases this can be done by simple measures, the most effective being encouragement to cough (see above) If the patient is not too distressed, coughing should be carried out in the prone position with the foot of the bed raised and the pillows removed, so that the bases of the lungs are uppermost This position is nearly always the correct one, since the bronchi to the lower lobes are most commonly obstructed Additional measures include hot drinks at frequent intervals and the administration of adrenaline and aminophylline if bronchial [illegible]

removing the obstructing secretions

Cyanosis and dyspnœa frequently occur when a major bronchus is obstructed and call for the administration of oxygen continuously Morphine in small [illegible]

PULMONARY EMBOLISM AND INFARCTION

In the majority of cases the pathological process [illegible]

as they are in the prevention and treatment of venous thrombosis. Accordingly, it has been decided to include the treatment of pulmonary embolism and infarction in the section devoted to diseases of the blood vessels on p. 623 (see also p. 92).

INTRATHORACIC NEW GROWTHS

MALIGNANT TUMOURS

Bronchial Carcinoma.—There is no doubt that the prevalence of bronchial carcinoma has been rising steeply during the past twenty-five years. *In men* it now exceeds pulmonary tuberculosis as a cause of death in Great Britain, and has become the commonest type of malignant tumour. Hopes for its prevention are at present based on the view that it is caused by the smoking of tobacco, especially cigarettes, and possibly by pollution of the atmosphere by the products of incomplete combustion in industrial cities and towns. If that is proved, the disease is at least in theory preventable. Even in our present state of knowledge it is probably fully justifiable to dissuade all young persons from ever starting to smoke tobacco.

Treatment.—Radical surgery affords the only prospect of cure. Provided the operation can be undertaken before the tumour has extended beyond the lung, the number of successful results is by no means negligible, 25 to 30 per cent. of cases surviving for more than five years. The number of patients in whom operative treatment is practicable is, however, extremely small, probably only between one-tenth and one-fifth of all cases. Generally this is because the tumour has reached too advanced a stage before it is suspected, but operative treatment may also be prevented by old age, poor general condition or respiratory insufficiency

As soon as the diagnosis is made, whether conclusively by bronchial biopsy or presumptively from the radiological appearances, a decision must be taken [illegible]

function. Surgical treatment is contra-indicated by :

1. Serious cardiovascular or renal disease.
2. Distant metastases, the commonest sites being the supraclavicular lymph nodes, the liver, the skin, the brain and the skeleton.
3. Severe impairment of respiratory function, which is usually due to chronic bronchitis, asthma or emphysema.
4. Invasion of the mediastinum as shown by paralysis of either hemi-diaphragm or of the left vocal cord, Horner's syndrome, a brachial plexus lesion, localized displacement of the œsophagus, or obstruction of the superior vena cava or trachea.
5. Direct or metastatic involvement of the pleura, which, in doubtful cases, may have to be confirmed by thoracoscopy.
6. Proximity of the tumour to the main carina, making its resection technically impossible.

If none of these contra-indications is present, the patient should be referred to a surgeon for thoracotomy. Pneumonectomy is generally the operation of choice, but if the lesion is localized to a single lobe, a lobectomy may be performed, particularly if the patient is over sixty-five years of age or if his respiratory function is impaired. In expert hands the risks of the operation itself are

slight, but even after a technically successful pneumonectomy or lobectomy the tumour recurs in about 70 per cent. of cases within five years

Palliative Treatment.—If the case is not suitable for surgical treatment, radiotherapy may be given. Although this has seldom succeeded in prolonging life, better results may yet be achieved by such apparatus as the linear accelerator, which allows much higher doses to be applied without damage to the skin or superficial tissues. Even with the apparatus in current use a valuable, although temporary, degree of symptomatic relief can sometimes be obtained, particularly for distressing symptoms caused by superior vena caval obstruction, tracheal compression and pain due to invasion of the chest wall or to skeletal metastases. Occasionally, too, radiotherapy may relieve repeated hæmoptysis, or bronchial obstruction with its sequelæ of pulmonary atelectasis and suppuration Sooner or later symptomatic treatment will be required for the relief of pain, cough and breathlessness Drugs such as the compound tablet of codeine, methadone and pethidine should be used initially, but later most patients will require opiates which also relieve anxiety A mixture containing morphine, 15 mg (¼ gr.), and cocaine, 10 mg (⅙ gr), flavoured with sugar and alcohol is often remarkably effective in relieving pain and raising morale. This mixture may at first be required only at night, but later increasing doses may have to be given every few hours. Ultimately, increasing doses of morphine by hypodermic injection are necessary. Chlorpromazine is sometimes of value in the relief of pain and mental distress and may be prescribed either before opiates are used or in combination with them, it may also be valuable in suppressing nausea and vomiting.

NON-MALIGNANT TUMOURS

Bronchial Adenoma.—This tumour generally consists of a small intrabronchial lesion with a large encapsulated extra-bronchial extension. The portion of the tumour situated within the bronchial lumen can be removed through the bronchoscope, but, as the extra-bronchial extension remains, recurrence is almost invariable It is therefore necessary to resect the pulmonary lobe or segment containing the tumour along with the bronchus from which it arises.

Benign Mediastinal Tumours and Cysts.—These should generally be removed surgically as soon as they are discovered because most of them produce symptoms sooner or later. some do so by their size alone; others become infected and a few undergo malignant change The operative mortality is very small.

PNEUMOCONIOSIS

Although in the past the term pneumoconiosis was used to include all diseases of the lungs due to the inhalation of various kinds of dust, it is now normally reserved for diseases due to silica, asbestos and coal dust.

The prevention of these conditions is closely bound up with the technical prob[…] of devising measures for reducing the concentration of dust in the air and […] the intelligent co-operation of b[…] workers In addition, […] the best results are to be achieved. […] strongly advised

taken, further deterioration is inevitable, whereas if exposure to dust is stopped at a fairly early stage the advance of the disease may in some cases be halted.

In the case of coal-workers' pneumoconiosis, however, the position in this

employment and the dislocation of family life which result from such a change place a heavy load of responsibility on the doctor who advises a man to leave the pits. The decision should usually be made by a chest physician, who will give consideration not only to the patient's medical condition but also to his social and economic circumstances

The symptomatic treatment of pneumoconiosis differs in no essential respect from that of chronic bronchitis (p. 656) and emphysema (p. 658).

FUNGOUS INFECTIONS OF THE LUNGS

These conditions, which are all rare, include:

1.
2.
3.
4.
5.
6. Moniliasis (*Candida albicans*).

Aspergillosis and moniliasis are essentially saprophytic infections of devitalized lung tissue They thus almost invariably occur as complications of diseases such as tuberculosis or bronchiectasis and are particularly prone to develop if [illegible] treatment with "wide spectrum" [illegible] ed must be stopped immediately [illegible] ins. A localized lesion heavily [illegible] example, have to be resected.

The other fungi are true pathogens and each can produce characteristic [illegible]

bacteriological assistance is available The infection usually responds [illegible]

Farm workers exposed to the dust from mouldy hay or straw may develop respiratory illness, the clinical features of which include cough, sputum, breathlessness on exertion and, in the more acute cases, pyrexia. Radiological examination of the lungs may show diffuse fine mottled opacities, and in chronic [illegible] farmer's lung is

from contact with the dusty hay or straw Penicillin or another antibiotic should be used to control the secondary bacterial infection which commonly occurs. A linctus containing codeine or methadone may be given for unproductive cough; methadone, 2·5 mg. three or four times daily, will usually be found the more effective

SARCOIDOSIS

Sarcoidosis is a disease which histologically resembles tuberculosis and which, in the opinion of some authorities, may represent an atypical reaction of the tissues to the tubercle bacillus Although it differs histologically from tuberculosis only in the absence of caseation, clinically it is a more benign illness. It can affect almost any organ in the body, but is particularly liable to involve skin, lymphatic glands, lungs, parotid glands and the uveal tract. It is, however, unusual for the disease to manifest itself in all these situations in any single case. The three commonest presenting features are · (1) bilateral enlargement of the hilar glands, usually detected on routine radiological examination but sometimes associated with erythema nodosum, (2) bilateral iridocyclitis; and (3) specific skin lesions such as cutaneous sarcoids or lupus pernio.

The diagnosis can usually be suspected from the distribution of the lesions in association with a low degree of tuberculin sensitivity and can sometimes be confirmed by biopsy of the skin, of a superficial lymph node or of the liver.

In most instances the disease resolves spontaneously after a course lasting months or years The only therapeutic agents known to influence sarcoidosis are cortisone and corticotrophin In view of the possible relationship of the disease to tuberculosis, anti-tuberculous chemotherapy (p 124) should always be given concurrently. Although hormonal therapy cannot cure sarcoidosis, it is undoubtedly capable of suppressing its more florid manifestations until spontaneous recovery ensues It is thus of particular value when the disease involves organs such as the eyes, lungs or heart, in which it may produce serious and possibly irreversible impairment of function Prolonged pyrexia is another indication for hormonal therapy In all other cases of sarcoidosis it is both unnecessary and unwise to embark on this expensive and potentially hazardous form of treatment.

Cases selected for treatment should be given prednisolone in preference to cortisone or corticotrophin The recommended initial dose is 5 mg four times daily by mouth Once the manifestations of the disease have subsided, the total daily dose should be reduced to 15 mg or even 10 mg It is impossible to generalize regarding the duration of treatment, but it should seldom be less than three months In all cases the drug should be withdrawn very gradually and its administration resumed immediately if symptoms return The most convenient form of anti-tuberculous chemotherapy to use in conjunction with prednisolone is a combination of PAS, 5 0 g, and isoniazid, 0 1 g., given by mouth twice daily.

[illegible]ONCHIAL ASTHMA

[illegible]chial muscles

[illegible]ent of the

TREATMENT OF THE ACUTE ATTACK

Minor attacks of asthma may be relieved by the inhalation from a hand nebulizer of a 1 : 100 solution of adrenaline or isoprenaline. Bronchodilator drugs which can be given by [illegible]

If the attack of asthma is of sufficient severity to require the attendance of a doctor, the following measures should be instituted. The doctor should go [illegible]

[illegible]

In view of the effectiveness of prompt treatment with adrenaline in reducing the severity of a paroxysm of asthma it is good practice to teach patients how to use a hypodermic syringe and to urge them to inject themselves as often as is required. Patients should be told firmly that no good purpose is served by delaying treatment, and that they are misguided in their determination to "fight off" an attack of asthma The earlier in the attack that adrenaline is given, the more effective will be its action. A small dose such as 0 2 to 0 3 ml [illegible] when many daily injections are given over a period of weeks, the patient appears to acquire a partial tolerance to the drug as shown by the poor effects produced even when large doses are given

Adrenaline should always be injected very slowly by the subcutaneous route. After introducing the needle under the skin and before injecting the drug, the piston of the syringe should be slightly withdrawn to make sure that the needle is not in a small vein, since the intravenous injection of adrenaline causes unpleasant reactions, e g tremor, bursting headache, faintness, palpitation or even collapse. Adrenaline loses its potency with keeping, particularly if exposed to the air or to sunlight. It should therefore be kept in tinted rubber-capped bottles in the dark, and even then should be renewed every three months.

In a small proportion of cases of great severity there is no response either to adrenaline or aminophylline. The term *status asthmaticus* is often applied to prolonged severe asthma of that type. The decision to transfer such a patient to hospital will depend on home circumstances, but there is no doubt that dramatic improvement often follows admission to a hospital ward, even if no other change is made in treatment If, however, the asthma persists, another intravenous injection of aminophylline should be given in the same dose as before, and this may be repeated at hourly or two-hourly intervals if necessary

Intramuscular injections of the drug are not so effective and are often painful.

The administration of adrenaline almost continuously is seldom as effective as the intravenous injection of aminophylline since many patients in status asthmaticus are "adrenaline fast", having already failed to respond to frequent injections of adrenaline. The method has, however, many advocates, and if it is used the following technique should be observed. A 1 ml. syringe filled with adrenaline solution should be strapped to the skin of the forearm after introducing the needle subcutaneously, 0.06 ml. (1 min.) should be injected every thirty to sixty seconds until relief has been obtained. As much as 7 ml. (120 min.) may be required in a severe case. Thereafter, to prevent a relapse, it is advisable to give 0.06 to 0.12 ml. (1 to 2 min.) every quarter of an hour for the next hour, twice in the second hour, and once an hour for another two or three hours. Alternatively, hyperduric adrenaline may be given by intramuscular injection. Absorption of the drug, which in this preparation is combined with mucic acid, is less rapid and its action is thus more prolonged. It can be given in a dosage of up to 1 ml. four-hourly.

When a patient with status asthmaticus fails to respond both to adrenaline and intravenous aminophylline, treatment with cortisone or corticotrophin often produces rapid and dramatic improvement, and is urgently indicated for all patients who are seriously ill. Either of the two drugs may be used. Cortisone is given by mouth in a dose of 75 mg. six-hourly on the first day, 50 mg. six-hourly on the second day and 25 mg. six-hourly thereafter. Corticotrophin is administered intramuscularly in the form of a gel, the usual dose being 30 to 60 units twelve-hourly for the first two days and once daily thereafter. In an average case the bronchospasm begins to subside within twenty-four hours of the start of treatment, but occasionally some degree of improvement is apparent as early as eight hours after the first dose. Although in some cases only partial relief of symptoms is obtained, a total lack of response is very uncommon. Treatment in all cases should usually be maintained for seven days, the drug thereafter being gradually withdrawn over the next two or three days.

The subsequent period of freedom from symptoms is variable and unpredictable. Some patients gain complete relief for many months, others only for a few weeks or even days. In general, the length of the remission seems to be related to the frequency of attacks prior to hormonal therapy, those patients who have been subject to frequent attacks having the shortest remissions. In many cases repeated courses of cortisone or corticotrophin are required at appropriate intervals, and in a few the remissions are so short that treatment may have to be maintained for an indefinite period. This method of using the hormones in chronic asthma is discussed on p. 693.

During any severe attack of asthma hot fluids sweetened with glucose should be given. It is rarely necessary to administer fluid intravenously. Oxygen therapy is indicated if cyanosis is present. Exhaustion through lack of sleep should be combated by the sedative effect of paraldehyde, 4 to 8 ml. intramuscularly. Morphine should never be used in asthma because of its depressing effect on the respiratory centre. Its use also involves a grave danger of death from asphyxia because the mucus which may be secreted after the spasm has been relieved will not be removed if the cough reflex has been abolished. There is, too, the liability to habit formation. Powerful hypnotics of the barbiturate group also have a depressant action on the respiratory centre and large doses should [...]ment of status asthmaticus

Infection may have been the precipitating factor in the production of the asthmatic attack or it may develop as a complication. Its presence is indicated by the expectoration of purulent sputum, which is only occasionally accompanied by frank manifestations of infection, such as pyrexia and leucocytosis It must always be treated promptly and vigorously.

When the paroxysm has been relieved, the patient should be given ephedrine hydrochloride by mouth in a dose of 30 to 60 mg. (½ to 1 gr.) thrice daily. The so-called antispasmodic cough mixtures containing lobelia, stramonium, belladonna or potassium iodide have little if any effect in controlling or preventing bronchospasm, and their use is not recommended. If the attack has been severe and prolonged, the patient will be exhausted and should be advised to stay in bed for twenty-four hours or longer. He should take a light, easily digested diet in small quantities at two-hourly intervals. It is particularly important that his main meals should be taken in the early part of the day; and when he settles down to sleep at night he should be fasting

THE MANAGEMENT OF THE ASTHMATIC STATE

"Many physicians feel their responsibility ended after the control of the acute paroxysm" (Coca)

This attitude cannot be too strongly deprecated to-day in view of the advance of knowledge regarding the factors which underlie the asthmatic constitution. Every effort must be made (1) to ascertain the immediate exciting cause of the paroxysm; (2) to determine the ætiological factors; (3) to institute therapeutic measures to prevent recurrence or, if this is impossible, to diminish the number and severity of the attacks

The management of the asthmatic state does not consist merely of giving a spasmolytic drug, but entails taking a careful clinical history and making a full

reserve.

While for clearness of description the ætiological factors must be separately considered, in practice they frequently occur in combination. In long-standing cases it is usually necessary to deal with several factors, e.g. psychological, allergic, infective and nasal, each playing a part in maintaining the asthmatic state. Hence treatment is often unsuccessful because one factor has received exclusive attention. The importance of the combination of factors is well exemplified by the story of Trousseau He found that contact with stable dust brought on mild asthma (the allergic factor) If, however, he lost his temper with his coachman in the stable where he was in contact with dust, an extremely severe paroxysm of asthma occurred (the psychological plus the allergic factor). Anger when he was out driving with his coachman did not induce asthma.

The Psychological Factor

In our experience the most important single factor in asthma is the psycho- emotional

a is in a

of minor

stimuli. If we accept the constitutional basis of asthma as being of great

importance, we can understand the danger of using the word "cure", since the removal of some abnormality in the nose or the correction of some dietary indiscretion may temporarily relieve the asthma but will leave unchanged the underlying constitutional basis. It is not surprising, therefore, that asthma may again occur when the broncho-constrictor centre is irritated by other stimuli.

It should be noted that the broncho-constrictor centre, which for constitutional reasons is excessively irritable, will react to psychological stimuli of a degree insufficient to have any effect on normal people.

The importance of the psychological factor in asthma has now been fully realized. It is the influence of this elusive factor which makes it so difficult to assess the value of any one therapeutic measure. It has long been known that the majority of cases of asthma cease having attacks on entering a hospital ward and often promptly relapse on returning home. The enthusiastic believers in allergy would suggest that the results depend on the removal of the patient from contact with some sensitizing allergen. We believe that in the majority of cases the results are effected by the psychological influence of white-coated doctors and efficient sisters, which inspires hope that something definite is being done to improve his condition. In addition, he is transferred to a tranquil environment from one which may have kept him in a state of nervous tension. The patient's skin reaction may have been positive to dust, feathers, etc., before he entered hospital and will continue to be positive while he is free from asthma in the hospital ward, even though he is sleeping peacefully on a feather pillow. Any treatment involving injections or special manipulations is calculated to inspire confidence in the patient. We, like others, have obtained excellent results in the management of the asthmatic state by injections of distilled water. Since 50 to 60 per cent. of all asthmatics can be improved by a simple spasmolytic drug and cheerful encouragement by the family doctor, it follows that the claims made for many forms of treatment commonly employed today must be accepted with due reserve.

The following case histories are given with the object of illustrating the psychological factor in asthma.

Case 1. Mrs A., an asthmatic of long standing, had severe attacks periodically. She had lived in the same house for many years. No evidence of allergy was obtained from the clinical history or from skin tests. Her married life had always been unhappy owing to her belief that she was of inferior social status to her husband. Her sexual life had also been unsatisfactory, although she was the mother of two healthy daughters. A careful analysis of her asthmatic attacks indicated a close association between the paroxysms and her exacerbations of fear and loathing of her husband. During his absence abroad her asthma quietened down to a mild chronic condition, but anything which brought his presence back to her mind would start a paroxysm, e.g., a conversation with a friend, or reading in a newspaper about his career. The receipt of any letter from him, particularly if it contained any suggestion that he would be coming home on leave, was sufficient to induce a severe attack of asthma, which lasted for several days despite the repeated injection of adrenaline. All efforts at curing the patient failed, as she would neither accept the situation nor agree to a divorce. Possibly if the psychological aspect had been treated many years previously, results would have been different.

Case 2. A boy aged sixteen, the son of brilliant parents, had had periodic attacks of severe asthma since the age of six. He had eczema in infancy and there was a family history of asthma on his father's side. Skin tests were positive to horse and cat hair, dust and pollen, but negative to all ingestants tested. He had received many kinds of treatment, including non-specific desensitization. His feather pillow had been replaced by one of foam plastic. Periodic attacks of asthma continued just the same. Our analysis of the events immediately preceding his attacks made it clear that anything which induced a state of nervous tension would precipitate an attack. One day the boy's mother telephoned one of us that he had severe asthma. Inquiry elicited the information that he had been sitting examinations for the preceding three days. An assurance [illegible] would immediately subside without any treatment when the results of the examina- [illegible] if he had done well, was justified by its immediate cessation

allergic factor without correcting the underlying psychological factor is in our experience one of the main reasons why disappointing results are so frequently obtained in the treatment of asthma.

Assessment of the Psychological Factor.—*For the assessment of the* importance of the psychological factor, information regarding the following points must be obtained · (1) personal relations with family and friends; (2)

difficult to adapt himself to his social environment. The patient may have been "nervous" as a child or the family history may be "neuropathic".

We agree with Halliday that it is highly important for the doctor to make *full enquiries into the following three points:*

1. What kind of person is this? Is he over-agressive, emotionally unstable, shy and seclusive, etc?
2. Why did he take ill when he did? Inquiries should be made with regard to the mode of behaviour and psychological factors operating at or before the time of the *first* attack of asthma.
3. What is the person getting at?—i e. for what end or purpose is this behaviour? An attack of asthma may enable a person to attain what he desires or to avoid something which is unpleasant

Should the above investigations reveal a psychological element of importance, much can be done by the intelligent practitioner to improve matters. This is particularly the case in children.

Children.—The situation must be explained to the mother, so that her natural desire to protect the child may not defeat its own object by inducing a state of nervous tension. Often the mother herself is in a state of nervous tension which is unconsciously transmitted to the child This aspect is often not fully appreciated, and successful results may not be obtained in the treatment of the child if the psychological factor in the parents is neglected. Parents are

must be corrected. There must be no suggestion that he is "delicate" and different from other children, and he must be induced to play with them in order to gain confidence. He must not be withdrawn from school for mild attacks, otherwise he might use his asthma as a means of avoiding his responsibilities. If the father has adopted a domineering attitude, this must cease. It is important to get the school-teacher to co-operate in these efforts.

results either because of inability to obtain the a child-guidance clinic

Adults.—A different method must be adopted for treating the psychological elements in adults

Careful questioning will frequently reveal a state of mental conflict or anxiety in the patient, consequent on unhappy relations between husband and wife, parents and children, employers and employees, etc. Any cause of anxiety, however, may start an asthmatic attack. For instance, one of our patients, who

ialine, told us that on one occasion

The terror induced by the mere

sufficient to induce a paroxysm of

asthma. In other cases, the attack of asthma is used by the patient as a means of escape from performing duties which he finds to be unpleasant, or for the acquisition of sympathy. The family doctor, by the use of explanation and

effect in the production of asthma, is not infrequently sufficient to relieve nervous tension and to produce improvement. In some cases, however, the psychological factor is so complex and so deeply ingrained that it is necessary to refer the patient to a psychologist.

The Allergic Factor

A state of inher

present in asthma

ally it may be a dr

difficult, since sensitivity to a substance may vary from time to time for reasons not clearly understood.

In investigating the allergic factor it is essential to obtain a careful history of how and when the original attack of asthma began. In general, it may be said that the earlier in life asthma commences the more often will an allergic factor be found. This probability is increased by the coexistence of eczema, urticaria, prurigo, hay fever or migraine, or by a family history of allergy.

The allergen may be absorbed by ingestion or inhalation. The alimentary rout

asth

pota

In childhood and early adult life, inhalants are of considerable ætiological importance. The chief inhalants are animal emanations, such as horse dander and feathers, cat and dog hair, pollens, moulds and orris root, which is used frequently

patient's statement too easily. Again and again we have had patients who claimed that certain articles of food or some animal emanation produced an asthmatic attack, and yet, when the supposedly offending article was brought into contact with the patient in a disguised form, no asthma resulted. Such experiences suggest that the patient's deductions are often at fault in assessing the part played by any factor in starting an asthmatic attack. In other cases the asthma results from psychological causes, as exemplified by the story of the patient who believed that her asthma was due to emanations from roses and immediately had

an asthmatic attack at the sight of an artificial rose. Nevertheless, the doctor should make an effort to discover an allergic factor in every case of asthma, particularly in children. In addition to taking a careful history it may be necessary to make skin tests with solutions of the common inhalants and ingestants which can be obtained from manufacturers, such as Bencard and Co. Ltd.

Intradermal Test.—The most satisfactory test is made by introducing 0·01 to 0·02 ml. of the solutions of extracts to be tested into the skin of the volar surface of the forearm. A control injection of carbol-saline is also made. A positive reaction is recognized by the appearance within ten to fifteen minutes of a wheal of at least 5 mm. in diameter. Pseudopodial extensions from the wheal indicate definite sensitivity.

Scratch Test.—Another method of skin testing is to place the solution of the extract on the skin, which is scarified through the drop with a needle.

Interpretation of Skin Tests.—The interpretation of the clinical significance of the skin tests is far from easy. A patient may give a history of

tests indicate that the sensitizing agent is an ingestant or an inhalant, measures should be instituted which will enable the patient, if possible, to avoid contact with it

Ingestants.—If the allergen is some uncommon food such as strawberries, pork or shell-fish, its recognition is usually easy and its elimination from the diet

the clinical history and from the presence of strongly positive skin tests, feathers in pillows and quilts should be replaced by the best Java kapok. Horse-hair mattresses should be covered with rubber sheeting or replaced by the sorbo rubber mattress as supplied by the Dunlop Rubber Company. If sensitivity to cat or dog hair is suspected, these pets should be removed from the home. These changes should only be advised if the asthma is not controlled by the other measures described for the management of the asthmatic state, nor should an unduly optimistic attitude be adopted, since in our experience the results are not infrequently disappointing.

A dusty atmosphere undoubtedly predisposes to attacks of asthma, but whether this is due to sensitivity to allergens in the dust or to mechanical

irritation of the respiratory mucous membrane we are not prepared to say. In either case, the less the patient comes in contact with a dusty atmosphere the better. Accordingly, the minimum of furniture should be kept in the bedroom and a vacuum cleaner should be used for removing dust from the floor, crevices and ledges.

If the patient is sensitive to orris root, then face powders must be prohibited or special preparations free from orris root used These may be obtained from any chemist (Queen products).

[illegible]

be advised

Specific Desensitization.—Should the patient find it impossible to avoid the offending allergen, desensitization may be attempted In the case of [illegible]

increased Desensitization is much more frequently employed against inhalants. When sensitivity is multiple it is advisable to use a solution containing a mixture of the commoner inhalants, e.g feathers, dust, animal hair and orris root A mixed inhalant solution, with full directions, may be obtained from C. L. Bencard, Minerva Road, Park Royal, London, N W 10 Specific desensitization is most likely to be successful where only one allergen is concerned It has certain risks, fortunately rare, and should not be practised by those unfamiliar with the technique. In our experience the benefits claimed to result from specific [illegible]

theless, specific desensitization is believed to be of value by many authorities, and occasionally a long period of relief may follow this form of therapy.

Non-specific Desensitization.—For this purpose many substances have been used, such as peptone, tuberculin, milk, TAB vaccine, sulphur, auto- [illegible]

have been overlooked.

The Infective Factor

An acute respiratory infection will precipitate or aggravate an attack of bronchial spasm in the majority of asthmatics. Such attacks may be prevented or rapidly controlled by adequate treatment of the infection. Accordingly, the measures already described for the prevention and treatment of acute respiratory [illegible]

temporary benefit often follows, relapse is all too frequent Vaccine therapy is not recommended.

The Nasal Factor

Sneezing, watering and itching of the nose often occur in asthmatics, particularly prior to the onset of the attack. The mucous membrane of the nose is boggy and pale in colour, indicating the presence of an allergic factor (allergic rhinitis). For temporary relief of symptoms the instillation of ephedrine nasal drops is effective (see p. 646).

Abnormalities such as polypi, deflected septum and hypertrophy of the turbinate bodies, enlarged adenoids and tonsils are commonly present and may interfere with free ventilation of the nose. Experience has shown, however, that the effect of surgical treatment of these abnormalities on the asthma is most disappointing. The principle which we advocate is that radical surgical treatment should be advised only if such treatment would have been indicated in a patient without asthma.

Infected antra should be treated in the first instance by proof-puncture and lavage rather than by open operation.

Drugs

Sedative Drugs.—Many asthmatic patients, particularly those in whom the psychological factor is prominent, live in a state of constant nervous tension. For such persons phenobarbitone in small doses of about 30 mg. (½ gr.) night and morning is of value.

Spasmolytic Drugs.—Chronic asthmatics, who have failed to respond to the various forms of treatment outlined above, may be instructed to inject themselves with adrenaline, the most useful drug available for the treatment of asthma. By this means many patients, who would otherwise be semi-invalids, can be enabled to live a practically normal life. A dose as small as 0.1 ml. (2 min.), if given at the onset, may be sufficient to abort the attack. The patient should discover for himself the smallest effective dose. In general, however, some degree of tolerance develops and it will be necessary, as time goes on, to increase the dose gradually. In addition, the knowledge that severe attacks may be prevented restores confidence, which so many asthmatics have lost. An injection of Hyperduric adrenaline, 0.5 to 1 ml., given in the evening may procure freedom from bronchospasm during the night. Isoprenaline sulphate is very effective in relieving bronchospasm in some patients. The drug is administered sublingually in 10 to 20 mg. tablets. Unfortunately, palpitation is often a distressing side-effect.

Although treatment is only palliative, a spasmolytic drug, if persistently used for several months, may lessen the frequency and severity of the attacks. The most suitable for this purpose is ephedrine hydrochloride, which can be given by mouth in a dosage of 30 to 60 mg. (½ to 1 gr.) two or three times a day for an

the drug tends to cause sleeplessness, the last dose should be taken at least four ... may be prescribed with a barbiturate

troublesome is dysuria—the result of

If this occurs, treatment should be discontinued for a few days but may be resumed later, using smaller doses. A similar policy should be adopted if palpitations or sweating develop.

Aminophylline, by mouth in doses of 0·2 to 0·6 g. (3 to 9 gr.) three or four times daily is sometimes effective in controlling spasm. Unfortunately, the higher dosage which some patients require is often not tolerated owing to gastric irritation

driven by an electric motor. Alternatively, a cylinder of oxygen may be used.

nebulizer gives considerable confidence and helps to relieve anxiety and tension.

Cortisone and Corticotrophin.—In some cases of asthma, particularly those associated with chronic bronchitis, breathlessness and wheeze may continue for weeks or months unrelieved by spasmolytic drugs or by the control of respiratory infection with antibiotics. These patients are often seriously

for the more acute asthmatic episodes. In exceptional cases the treatment may

without delay.

Other Drugs.—Morphine, in the management of the asthmatic state, is contra-indicated because of the danger of habit formation. The catastrophic consequences of using the drug in asthmatic attacks have already been emphasized (p. 685).

Calcium has been employed in many forms in the treatment of asthma, but there can be no doubt that it is of little value.

Antihistamine Drugs, so valuable in the treatment of superficial allergies, are of little use in the treatment of asthma

GENERAL MEASURES

Apart from the investigation and treatment of the special factors already described, the family doctor can always give valuable help by his commonsense

must be treated on its own merits.

rewarding policy. Thus, nearly all asthmatics insist on sleeping in a cool, well-ventilated bedroom. Hence if the patient is to avoid the paroxysms of

warm room to a cold

particularly cold or

If coughing begins

should therefore be

is of limited value in

carries serious risks

mimetic amines are less satisfactory during the night for the reasons already stated Many asthmatics have their favourite ritual for coping with an attack, and such procedures should not lightly be abandoned. Ten to thirty minutes may elapse before the symptoms subside and the patient is able to settle down

patient may develop a technique for aborting a nocturnal paroxysm of asthma without disturbing any other members of his household. The preparations

4 to 8 ml (60 to 120 min.), or

n.).

matics do best if they take a

A heavy meal before retiring

bronchial spasm. Flatulent

to play an important part in asthma. In general, it may be said that a cool dry climate without marked

Many asthmatics

3,000 ft. It has

mical changes in

to us that some at least of the benefits credited to a change of climate have in reality a psychological basis.

claim remarkable beneficial

ther administered internally,

effects are certainly frequent,

largely due to the improvement in the patient's general health and mental outlook which result from a holiday under pleasant conditions, and from the unintentional psychotherapy of the enthusiastic spa physician.

Prevention of Upper Respiratory Infections.—In the majority of sufferers the occurrence of any respiratory tract infection will precipitate an asthmatic attack. It is of the utmost importance, therefore, that every care

should be exercised in their prophylaxis and treatment. Preventive measures have been fully described on p 648.

[illegible]

become " upper thoracic " in type—a sign characteristic of the emphysematous asthmatic. For the treatment of these conditions postural and breathing exercises are of paramount importance, and a large proportion of chronic asthmatics will derive benefit by undertaking them This necessitates the help of a qualified physiotherapist, not only to give instruction in the physical exercises but to loosen the stiff thoracic muscles by applying massage The book published by the Asthma Research Council, entitled " Physical Exercises in Asthma ", fully describes suitable exercises in detail (obtainable for 2s. 3d. post free from H. K. Lewis & Co., Gower Street, London, W.C. 1).

PAROXYSMAL RHINORRHŒA

This term is used to describe a clinical state characterized by paroxysms of sneezing and watery discharge from the nose due to an excessive vasomotor reaction to a variety of stimuli These may be bacterial, thermal, emotional or allergic in origin. As in asthma, two or more factors may operate simultaneously and the relative importance of each varies from case to case. Paroxysmal rhinorrhœa may occur only at a specified season of the year, in which case the condition is called seasonal paroxysmal rhinorrhœa, of which the chief example is hay fever, or it may occur at any time throughout the whole year, in which case it is often called perennial paroxysmal rhinorrhœa A family history of paroxysmal rhinorrhœa and evidence of emotional instability are commonly found in both the seasonal and perennial groups

SEASONAL PAROXYSMAL RHINORRHŒA

Hay Fever

Hay fever occurs in persons who are hypersensitive to the pollen of grasses and is characterized by itching and watering of the eyes, sneezing and running at the nose, and a hacking cough

The hay fever season usually starts in the South of England about the middle of May and continues throughout June and July. In Scotland, the season is two or three weeks later. In America and other countries hay fever is frequently caused by the pollen of trees and shrubs Allergic symptoms to the pollen of ragweed are common in the United States, usually from August to October.

Symptomatic Treatment.—*General Measures.*—There is no doubt that the use [illegible]
of hay [illegible]
(Anthi [illegible]
dose o [illegible]
variati [illegible]
necessary to try the effect of different preparations in an individual case. Complete relief or considerable symptomatic improvement following their administration

can be expected in over 80 per cent. of cases. In severe intractable cases which do not respond to treatment with antihistamine drugs, it may be justifiable to give a course of cortisone orally or corticotrophin gel intramuscularly, on the lines indicated for asthma on pp. 87, 685.

When the grasses are pollinating, the sufferer from hay fever should avoid country districts where the air is heavily laden with pollen, but pollen is so widely disseminated that severe symptoms may occur in the middle of a large city. In a severe uncontrolled case it may be necessary to remain indoors with

for adrenaline and may be instilled into the eye in a strength of 0·1 to 0·2 g. (2 to 3 gr.) to 30 ml. (1 fl. oz.) of saturated boric solution.

The troublesome sneezing and irritation of the nose may be temporarily relieved by the instillation of ephedrine nose drops (N.F.) or by the application to the surface of the mucous membrane of the nose of an ointment containing chloretone 1 per cent. and ephedrine 1 per cent. A useful spray consists of 1 per cent. ephedrine sulphate in saline. Amphetamine, which is supplied in inhalers,

are effective in a high proportion of cases, pre-seasonal specific desensitization is not now so frequently required. The method entails the subcutaneous injection of pollen extract in increasing quantities before the onset of the hay fever season. Suitable extracts may be obtained from leading manufacturing firms (Parke, Davis & Co.; Duncan & Flockhart; etc.). The results of pre-seasonal desensitization have varied in the hands of different writers, but it

however, return to their former condition, requiring further desensitization.

Treatment must be started at least ten weeks before the beginning of the pollen season, i.e. *about the end of February or in the first week of March.* Details regarding dosage and method of administration are supplied by the manufacturers of pollen extracts.

To each injection, 0·1 ml. (2 min.) of adrenaline (1 : 1,000 solution) should be added in order to slow the rate of absorption and lessen the risk of a general reaction. After the injection the patient must be kept under observation for half

face, asthma or collapse occur, a further injection of 1 ml. of adrenaline must be given. If the patient is in a state of collapse, artificial respiration must be started at once and 5 to 10 ml. of nikethamide injected intravenously The occurrence of a general reaction calls for a reduction of the next dose of extract to one-quarter and this should be combined with 0 3 ml (5 min) of adrenaline. Subsequent doses must be increased cautiously.

Local Reactions are more frequent and are evidenced by redness, swelling ... ed not be inter- ... the subsequent

PERENNIAL PAROXYSMAL RHINORRHŒA

(Vasomotor Rhinitis)

... especially a ...

Sensitiv ...

combined ... there is no evidence of allergy and no satisfactory explanation for the vasomotor disturbance can be obtained.

The first step is to exclude from the patient's environment all allergens to which he shows hypersensitivity (see p 690).

Treatment with antihistamine drugs (mepyramine maleate and promethazine) should be tried in all cases, though the results are not as strikingly good as in hay fever. Should this fail, in severe cases a course of treatment with cortisone or corticotrophin "gel" should be given a trial (see p. 685). Symptomatic relief may continue for weeks or even months after treatment is stopped.

Care should be taken to avoid fatigue, worry and cold, which are important precipitating factors. Varnish, smoke and perfumes often act as mechanical irritants and are liable to produce an attack If the patient's work entails spending many hours in a dust-laden atmosphere, a change of occupation may be desirable

... satisfactory explanation can be relieved temporarily by linear cauterization of the inferior turbinate bodies with the electric cautery. Diathermy is sometimes used for the same purpose. Zinc ionization of the nasal mucous membrane is also of value. These measures, however, are less frequently used since the introduction of the antihistamine drugs and cortisone.

STANLEY DAVIDSON.
I GORDON.
I. W. B. GRANT.

RENAL DISEASES

NEPHRITIS

CLASSIFICATION

THE CLASSIFICATION of *nephritis has always been a most difficult* problem, but since the treatment of the disease is still very largely symptomatic, the absence of an ideal classification based on cause is of less importance than it might have been. The classification of Ellis, who [illegible]

[illegible]

into this or any other classification. It is to be hoped that *in spite of this* [illegible]

[illegible]

encountered most often in a child or adolescent, starting abruptly and characterized by proteinuria, hæmaturia, hypertension and œdema, along with general symptoms such as malaise, vomiting and headache. About 80 per cent of patients recover completely. A small number, less than 5 per cent., die in this acute stage of hypertensive encephalopathy, cardiac failure or renal failure and uræmia.

In a further small fraction, about 3 per cent, the œdema and hypertension persist and over a period of less than a year from the acute onset renal function fails progressively and death occurs from uræmia. This is termed *Subacute Nephritis.*

The remaining cases improve, all the manifestations disappearing except for protein, red blood corpuscles and casts in the urine. Persistence of these abnormalities six months after the onset constitutes *Latent Nephritis.* The more usual course thereafter is for gradual diminution in renal function to occur along with rise in blood pressure, azotæmia and finally death in uræmia. *This* syndrome is *Chronic Type I Nephritis* (chronic interstitial nephritis; azotæmic nephritis), and its development is usually a slow process of five, ten or more years' duration. The latent stage ends when blood pressure begins to rise and renal function to deteriorate, and the patient is then considered to have chronic nephritis. Justification for the use of the term "latent" lies in the fact that complete recovery is still possible up to two years from the acute *onset.*

Type 2 Nephritis (hydræmic nephritis: chronic parenchymatous nephritis: nephrotic nephritis: nephrotic syndrome: nephrosis) is characterized by an insidious onset, with œdema as the presenting symptom. Œdema may last for months or years *and commonly amounts to anasarca.* The condition is commoner in children than in adults. In the initial stages, constitutional disturbance is absent and renal function is normal or but slightly impaired Massive proteinuria is usually accompanied by hæmaturia, but this is seldom

profuse, often only microscopical and occasionally absent. It may be intermittent. In the early stages hypertension is present in a minority of patients Prior to the discovery of antibiotics many patients died of intercurrent infection [illegible] in children In the majority, the course is that of progressive deterioration to death from renal failure over a period ranging from months to years.

BIOCHEMISTRY

For the proper handling of patients suffering from nephritis, some knowledge of renal function tests, and of changes in the blood constituents, is essential for guiding prognosis and treatment.

Renal Function Tests.—The simplest procedures, neither of which requires any special laboratory facilities, are the so-called "concentration" and "dilution" tests, both of which ultimately depend on careful estimations of the specific gravity of the urine In general practice the concentration test is all that is required, as the dilution test (not described here) gives no additional information. According to Fishberg, to carry out the concentration test the patient has breakfast with the usual amount of fluid, but has no more to drink until the test is finished next morning. Any urine passed on retiring or during the night is discarded Immediately after the patient is awake, twenty-two to twenty-four hours later, a specimen of urine is taken and another an hour later. Then the subject is allowed to get up and asked to walk about, a third and last specimen being obtained after another hour The specific gravity of the urine should normally be not less than 1·022 in one of the three specimens and opportunity can be taken to determine on the last specimen whether proteinuria is functional (see p. 718). With very severe renal impairment the specific gravity does not rise above 1 010. The range of 1 010 to 1 021 represents lesser degrees of damage. In œdematous subjects, the test should not be used because of the possibility of movement of fluid to or from the tissues masking the concentrating capacity of the kidneys. Patients can carry out this test in their own homes and take the specimens to the doctor. If a patient is unable to abstain from drinking because of thirst it is often an indication of advanced renal impairment of which there is usually other evidence. It is dangerous to ask a patient to abstain from fluids for twenty-four hours when his blood urea concentration is greater than 100 mg. per 100 ml.

The concentration test gives an indication of renal impairment earlier than the urea clearance test or the estimation of the blood urea. The fallacies in regard to œdema have been already mentioned. In estimating specific gravity, the urine should be at room temperature. The urinometers commonly supplied may be grossly inaccurate, and it is necessary to buy good ones or to have them checked, preferably against a Westphal balance in a laboratory. Allowance must be made for gross proteinuria, an amount equivalent to 10 g. per litre raising the specific gravity by 0 003.

The urea clearance test of Van Slyke should be preferred when œdema is present. In acute nephritis damage is sometimes confined to the glomeruli for a few days, tubular function remaining normal and urine of a high specific gravity being excreted. Simple estimation of the blood urea gives the best gauge of renal function at this stage If these causes of fallacy are excluded,

impairment of renal function in Bright's disease will be detected most readily by the concentration test. When the condition progresses unfavourably the clearance of urea diminishes and, last of all, the blood urea rises. In acute

to empty the bladder completely. Failure to do so invalidates the test and a catheter must be used. Even so, the bladder is not invariably emptied and the test is more reliable in those who are not confined to bed. The normal range with this test is a wide one, varying with diet and other factors. A figure below 60 per cent. of the average normal indicates renal impairment, while levels below 10 per cent. are found in uræmic patients. The test detects renal impairment when the blood urea is still within the normal range, and the urea clearance may be as low as 50 per cent of normal when the blood urea is still under 40 mg. per 100 ml. Whichever test is chosen, it must be remembered that repetition at appropriate intervals gives more information than a single observation.

More recently, clearance tests with substances such as inulin and diodone have been devised whereby the functional capacity of glomeruli and tubules can be separately assessed. These procedures are time-consuming and require elaborate laboratory facilities. Valuable information has been gained in the field of research, but at the moment clearance tests of this type must be con-

however, the development of subacute nephritis should be suspected.

In chronic nephritis, as renal function deteriorates the blood urea rises progressively until death occurs in the syndrome called uræmia, but there is no fixed level of blood urea at which the clinical features of uræmia appear since these depend largely on electrolyte imbalance. The retention of waste products, predominantly acid, along with the inability of the kidney to form ammonia to neutralize these, leads to acidosis. This is conveniently measured by estimating the carbon dioxide combining power of the plasma—normal range 50 to 65 volumes per 100 ml. In acute nephritis, renal failure and uræmia are fortunately rare

Fall in the level of plasma albumin—hypoalbuminæmia—is a constant finding associated with the œdema of type 2 nephritis and that of subacute type 1 nephritis. The normal range is 4 to 5 5 g. per 100 ml. and œdema is usually present with values below 2 5 to 3 g.

TYPE 1 NEPHRITIS

ACUTE STAGE

Although there is no specific treatment for any form of nephritis, the *vis medicatrix naturæ* can be aided in several ways. It is particularly important that the measures available should be rigorously carried out in the acute stage of

type 1 nephritis. The prospect of recovery from the acute process is good in about 80 per cent. of cases; but there is evidence that it is less so in those patients whose treatment is unduly delayed.

Rest in bed, a suitable diet and good nursing are the main points in treatment. Since many patients feel well after the first few days, and some even throughout their illness, restrictions are found irksome. To ensure that they are enforced,

alone These observations should be made at the very start of treatment, and their repetition at intervals as long as abnormality persists allows treatment to be carried out with greater confidence

Rest in bed.—This is necessary to avoid chilling, since constriction of the skin capillaries is thought to be accompanied by constriction of those supplying the nephrons The patient should not be exposed to draughts. A single blanket round the body, flannel pyjamas and hot bottles should be used to conserve warmth.

Ideally, patients should be kept in bed until all abnormalities have disappeared. A minimum of four weeks in bed should be observed in all patients, even in the mildest case In a high proportion a time comes when recovery appears to be complete except for proteinuria, microscopical hæmaturia and perhaps a few casts. Since this state not infrequently persists for months, it is reasonable to allow the patient to get up if no further improvement is noted after two weeks. There is no proof that the likelihood of chronicity is increased

œdema, hypertension

protein, salt (NaCl) and fluid.

Restriction of protein is practised because the excretion of products of protein catabolism is impaired Carbohydrates and fat on the other hand are metabolized to carbon dioxide and water The sodium ion is a factor in the formation of œdema and must be excluded as much as possible from the diet by a careful selection of foodstuffs, by using no salt in cooking and by providing none on the meal tray. At the same time the intake of fluid in all forms is

of potassium—orange juice, for example, contains some 50 mg. per 30 ml.

of the illness and to a lesser extent on appetite. In any event, the caloric value will be initially below the basal requirement for the space of one or even

same time as the venesection, therefore, a sedative is given. Sodium phenobarbitone is best avoided owing to the state of the kidneys and 2 to 10 ml. of paraldehyde should be injected intramuscularly, not more than 5 ml in one site. If, in spite of this, convulsions develop or continue, injections of 1 to 5 ml. of paraldehyde should be given every two hours until they cease. Further treatment with paraldehyde depends upon the level of the blood pressure. While there are as yet few reports on the use of hypotensive drugs in the

I nephritis,
least where
ause further

methonium when the blood urea exceeds 100 mg. per 100 ml. unless other forms of treatment have failed to relieve the convulsions. When faced with this occurrence, hexamethonium bromide may be given intravenously, 2·0 mg. every

the injection and lowered if the fall in blood pressure is too great. After the desired fall is obtained, intramuscular injections of hexamethonium bromide should be given as necessary, controlled by observations on the blood pressure.

Acute Heart Failure.—This condition is less common than hypertensive encephalopathy but may occur along with it. Pulmonary œdema with dyspnœa and cyanosis and sometimes enlargement and tenderness of the liver are the signs. As a temporary measure in emergency, in addition to the subcutaneous

id

ia.

Diuretics are useless, and the same can be said of 4·285 per cent. sodium sulphate and 50 per cent. glucose intravenously. Recent records of the results of decapsulation of the kidneys confirm impressions that the operation is without value. The only course is to adopt the régime recommended for acute renal failure (p. 714) in the hope that the kidneys may resume their function. When the

glomeruli are primarily involved, however, experience has shown this to be improbable.

After-care of Cured Cases.—When, some time after the other manifestations have disappeared, the urine becomes free of protein, casts and red blood cells, relapse seldom occurs It is well, however, to take precautions for a year to avoid exposure leading to wet feet and wet clothes This may mean a change of occupation. Strenuous sports should be avoided for the same time. Parents who frequently ask advice about sea-bathing and sun-bathing should have these points brought emphatically to their notice No restriction of diet is necessary. After six months from recovery and again after one year a check should be made on the urine, blood pressure and renal function.

A history of nephritis is no contra-indication to pregnancy provided there is no renal abnormality still present. In latent or chronic nephritis there is a considerable chance of abortion, and as the renal condition is usually made worse, a close watch should be kept on the blood pressure and blood urea in order to decide whether termination of pregnancy is necessary

Subacute Stage of Type 1 Nephritis

This condition may be wrongly diagnosed as a severe attack of acute nephritis, showing marked œdema and hypertension, along with azotæmia and impaired renal function If the plasma albumin is estimated it is found to be less than 3 g. per 100 ml. Instead of the expected improvement which occurs in acute nephritis, the symptoms increase in severity, and death occurs in a few months from renal failure. Treatment is palliative, and difficult, because one is called on to treat simultaneously both the renal insufficiency and the œdema which is due largely to hypo-albuminæmia The diet suitable is the stage 2 diet for acute type 1 nephritis containing protein, 45 mg , sodium chloride, 2 g , and calories, 1,800 In view of the renal insufficiency, fluids are not restricted. A reduction in the serum sodium is an indication for including more salt in the diet. Those patients lose much protein in the urine, and if it is decided to give more protein in the diet, the effect on the blood urea should be watched A point is eventually reached when the measures used in the palliative treatment of uræmia become necessary.

The Latent Stage of Type 1 Nephritis

This condition is defined as the persistence, six months after acute nephritis, of excretion of protein, red blood cells and casts in the urine, when clinical and biochemical abnormalities have disappeared. The patient feels and looks well. Up to two years complete recovery is possible, but beyond that time persistence of the urinary abnormality indicates the development of chronic nephritis. In treatment, restriction of diet is unnecessary Respiratory infections should be taken seriously, the patient being put to bed and given antibiotics. Undue exposure to wet and cold should be avoided This is one type of nephritic patient in whom the advisability of tonsillectomy is often raised, but it is very doubtful if the operation has any influence on the course of the disease Every three months the blood pressure, urine and renal function must be checked

From time to time patients are found with proteinuria who give no history of previous acute nephritis, and at this stage the illness is often detected at examination for Life Assurance or National Service It is true that many of these patients have latent and chronic nephritis, but is is necessary to exclude functional proteinuria before making such a diagnosis (see p 718)

being determined by the level of the serum sodium. Relief of hyponatræmia in itself helps to diminish hyperkalæmia by inducing a better flow of urine.

Acidosis is treated with sodium bicarbonate by mouth or, if there is vomiting, [illegible]

[illegible] stage of renal failure and is characterized by increasing intensity of the manifestations which have been described. In spite of the best biochemical control there is inevitably a point when survival is no longer possible, and unless perhaps for an exacerbation in an early case from one of the temporary factors already mentioned, there can seldom be justification for adopting the measures advocated for the treatment of acute renal failure (p. 714). With dialysis, using the artificial kidney, the biochemical picture may be brought back towards normal and symptoms relieved for a period of weeks or even a few months. Deterioration inevitably follows and subsequent dialysis provides shorter periods of relief. Facilities for this treatment are not readily available. As a palliative measure for vomiting which is not due to some remediable biochemical abnormality or to hypertension, *chlorpromazine, 50 mg. intramuscularly three or four times* a day, is occasionally helpful. For headache and irritability *chloral hydrate, 1·5 g*, may be tried, or paraldehyde, but morphine will often be required. Diuretics [illegible] are contra-indicated.

characteristic of the group, e g. the large abdominal masses due to cystic kidneys. The symptomatic treatment is the same in all instances.

TYPE 2 NEPHRITIS

Type 2 nephritis runs a prolonged course lasting many months or even several years, and for a large part of this time œdema is likely to be present. Since no treatment has yet been proved to be curative, the measures used are directed very largely towards mitigating œdema, overcoming infection and maintaining the general condition in the hope that the renal lesion will eventually take a favourable turn.

The hypothesis generally accepted regards œdema as due to fall in colloid osmotic pressure of the plasma from loss of the albumin fraction of the plasma proteins into the urine, salt and water play an important but accessory part. Œdema is generally present when the plasma albumin level falls below 2·5 to 3 g. per 100 ml and on the other hand is generally absent when the level is over 3 g. The treatment of œdema is most simply considered under three headings: (1) prevention of water retention, (2) attempts to raise plasma osmotic pressure, and (3) removal of water by diuretics or by mechanical means.

Prevention of Water Retention.—The formation of œdema can be [illegible] of salt [illegible]

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exchange and absorbed, promoting acidosis, and because of this resins should not be used if renal function is abnormal. Potassium ions are also retained in the gut This drawback is only partly obviated by the incorporation of a potassium phase resin to the amount of 25 per cent. of the total, and fruit juices or additional potassium in other form should be given Hypocalcæmia is less common Close laboratory control is required if resins are used.

Attempts to raise the Colloid Osmotic Pressure of the Plasma.—This problem has been approached in several ways First by Epstein, who gave 200 g. or more of protein in the diet daily in the hope that plasma albumin might be synthesized more quickly than it was lost through the kidneys. Most authorities now agree that a rise in plasma albumin seldom follows the use of such a diet, even when the nitrogen balance is kept positive over periods of many weeks.

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use of these blood products involves some risk of homologous serum jaundice.

Substitutes for plasma are also used, one of which, acacia in 6 per cent solution, dates from the First World War Given by vein, this substance often promotes diuresis, but it lost popularity because it was shown to be largely deposited in the liver and was said to interfere with the synthesis of plasma albumin More recently other substitutes for plasma have been developed. Dextran—a polysaccharide consisting exclusively of dextrose—has been extensively used for the treatment of shock. Its action depends on the exertion of osmotic pressure while it remains in the circulation It increases the plasma volume and, when used with care, has a place in the removal of œdema.

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raised or more than microscopical hæmaturia present The xanthine group of diuretics is of no value. Acetazoleamide acts by inhibiting carbonic anhydrase. This enzyme takes part in the formation of carbonic acid in the tubules. In this process hydrogen ions are set free which are exchanged for sodium ions in the tubule fluid, in order to conserve sodium Acetazoleamide prevents this

become necessary.

Other Lines of Treatment.—Because the basal metabolic rate in a proportion of patients is low, and because the blood cholesterol is consistently high, thyroid extract has been extensively used. There is, however, no evidence that the very large doses which are tolerated by patients with type 2 nephritis have any influence whatever on the course of the disease Restriction of dietary fat because of elevated blood lipoids is without benefit to the patient.

It is well known that intercurrent acute infections, notably measles in children, are sometimes accompanied by a remission of type 2 nephritis Infec-

stage of renal failure and is characterized by increasing intensity of the manifestations which have been described. In spite of the best biochemical control there is inevitably a point when survival is no longer possible, and unless perhaps for an exacerbation in an early case from one of the temporary factors already mentioned, there can seldom be justification for adopting the measures advocated for the treatment of acute renal failure (p. 714). With dialysis, using the artificial kidney, the biochemical picture may be brought back towards normal and symptoms relieved for a period of weeks or even a few months. Deterioration inevitably follows and subsequent dialysis provides shorter periods of relief. Facilities for this treatment are not readily available. As a palliative measure for vomiting which is not due to some remediable biochemical abnormality or to hypertension, chlorpromazine, 50 mg. intramuscularly three or four times

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characteristic of the group, e g. the large abdominal masses due to cystic kidneys. The symptomatic treatment is the same in all instances.

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Transfusion with blood, plasma or plasma reconstituted in higher concentration has failed to increase the plasma albumin level. In the United States of America salt-free human serum is available in 25 per cent concentration with which diuresis can be induced, although without lasting alteration in the level of the serum albumin, and without effect on the course of the disease. The use of these blood products involves some risk of homologous serum jaundice.

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Removal of Fluid (Œdema).—Only the mercurials and urea are worth considering as diuretics and of these the mercurials are much the better, used alone or with an acidifying salt Urea is much less effective besides being very unpleasant to take These diuretics are contra-indicated if the blood urea is raised or more than microscopical hæmaturia present. The xanthine group of diuretics is of no value. Acetazoleamide acts by inhibiting carbonic anhydrase This enzyme takes part in the formation of carbonic acid in the tubules In this process hydrogen ions are set free which are exchanged for sodium ions in the tubule fluid, in order to conserve sodium Acetazoleamide prevents this [illegible]

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The manifestations described in this and the preceding section are common to gradual renal failure whatever its pathology and are seen in the later stages of nephritis types 1 and 2, chronic pyelonephritis, amyloid nephrosis, cystic kidneys and other conditions. There may also be present the specific features characteristic of the group, e.g the large abdominal masses due to cystic kidneys. The symptomatic treatment is the same in all instances.

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In the presence of marked anasarca, which does not yield to other measures, drainage by acu-puncture or by insertion of Southey's tubes at the ankles may become necessary.

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The steroid hormones corticotrophin and cortisone promote retention of sodium and water, but in type 2 nephritis while œdema as a rule increases throughout their administration, diuresis occurs in a proportion of patients when the administration of these hormones is stopped (see p. 711).

The Régime of Choice.—Before starting treatment it is essential to know if hæmaturia or hypertension is present. The plasma albumin should be estimated along with the blood urea, a urea clearance test carried out and the behaviour of the serum sodium and potassium watched during certain forms of treatment. These observations will have to be repeated at intervals of a week or a fortnight. Daily weighing should be done as a check on the behaviour of the œdema All urine passed must be collected and the amount measured every twenty-four hours. As a rough guide the protein lost in twenty-four hours should be calculated, using Esbach's method along with a knowledge of the volume of urine passed If the œdema is more than slight the patient should be kept in bed.

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Control of Œdema —Very commonly, in spite of rigid restriction of salt and water, œdema remains static. Sometimes œdema even increases to such an extent that some relief becomes a matter of urgency. The best diuretics are the organic mercurials; a course of mersalyl by intramuscular injection is often very effective. The technique is described on p. 871. In using the gluteal region for injection, particular care should be taken to avoid the sacral nerve Intravenous administration is contra-indicated in the treatment of renal œdema because of the possibility, admittedly slight, of sudden death in sensitized individuals, particularly those who have had previous treatment with a mercurial diuretic Acid salts, such as ammonium chloride, are very useful in enhancing the effect of a mercurial, and should always be tried when mersalyl given alone has failed The technique of their administration is described on p. 871. The practice of giving a single dose some hours before the injection of mersalyl is often unsuccessful in type 2 nephritis, possibly on account of the hypoalbuminæmia, and administration every four hours is preferable. If satisfactory diuresis does not follow the second injection of 2 ml. of mersalyl combined with ammonium chloride it is unwise to persevere Poor results are not unusual when the plasma albumin is very low Since mercury is liable to damage the kidneys, *mersalyl should not be used in the presence of azotæmia*, hypertension or more than microscopical hæmaturia Even in the absence of these manifestations there is no assurance that some renal damage may not be sustained which is not immediately obvious The decision to use mersalyl should, therefore, be made only after a most careful consideration of all factors, and some prefer to remove fluid from the body by other means The writer has seen no damage to the kidneys which could certainly be attributed to mersalyl By acu-puncture or scarification of the skin of the legs, or by insertion of Southey's tubes, one on each side of the ankles, œdema fluid may be drained from the subcutaneous tissues By using a cardiac bed and lowering its foot,

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The rise can be disregarded unless it exceeds 60 mg. per 100 ml. and is accompanied by a fall in the urea clearance. Increase in proteinuria does not call for reduction of the protein of the diet. Provided the criteria mentioned remain satisfied, the diet should be maintained in its entirety for so long as the plasma albumin is below 3 5 g. per 100 ml., and whether œdema is present or not. With a level above 3 5 g. restriction of salt and water may be discontinued. In favourable cases proteinuria alone may then persist for months, and it is [illegible] More often renal [illegible]

or disappears After months or years the patient dies of uræmia For these

unfavourable cases the treatment after disappearance of œdema is the same as for chronic type 1 nephritis (p 706).

On preliminary examination of patients with type 2 nephritis, there is often [illegible]

It is safer, therefore, to start with a low protein intake of 20 g for a week, using the stage 1 diet recommended for acute type 1 nephritis (Table A, p 720), and to add 20 g. of protein each week Each step is controlled by observations on the blood urea and urea clearance before further addition is made Deterioration is an indication calling for a reduction in the amount of protein allowed

Control of Œdema.—Very commonly, in spite of rigid restriction of salt and water, œdema remains static. Sometimes œdema even increases to such an extent that some relief becomes a matter of urgency The best diuretics are the organic mercurials ; a course of mersalyl by intramuscular injection is often very effective. The technique is described on p. 871. In using the gluteal region for injection, particular care should be taken to avoid the sacral nerve. Intravenous administration is contra-indicated in the treatment of renal œdema because of the possibility, admittedly slight, of sudden death in sensitized individuals, particularly those who have had previous treatment with a mercurial diuretic. Acid salts, such as ammonium chloride, are very useful in enhancing the effect of a mercurial, and should always be tried when mersalyl given alone has failed. The technique of their administration is described on p 871. The practice of giving a single dose some hours before the injection of mersalyl is often unsuccessful in type 2 nephritis, possibly on account of the hypoalbuminæmia, and administration every four hours is preferable. If satisfactory diuresis does not follow the second injection of 2 ml. of mersalyl combined with ammonium chloride it is unwise to persevere Poor results are not unusual when the plasma albumin is very low Since mercury is liable to damage the kidneys, mersalyl should not be used in the presence of azotæmia, hypertension or more than microscopical hæmaturia Even in the absence of these manifestations there is no assurance that some renal damage may not be sustained which is not immediately obvious. The decision to use mersalyl should, therefore, be made only after a most careful consideration of all factors, and some prefer to remove fluid from the body by other means The writer has seen no damage to the kidneys which could certainly be attributed to mersalyl By acu-puncture or scarification of the skin of the legs, or by insertion of Southey's tubes, one on each side of the ankles, œdema fluid may be drained from the subcutaneous tissues By using a cardiac bed and lowering its foot, gravity [illegible]
consid [illegible]
during [illegible]
is sorr [illegible]
tapping The appropriate method is described in the chapter on Technical
[illegible]

instances the remissions are short lived, but in a small proportion of the successes it is claimed that blood chemistry returns to normal and proteinuria disappears

tion with measles under cover of penicillin, and with malaria, has therefore been induced in a small series of patients and remissions reported. The results achieved do not justify the risks involved

The steroid hormones corticotrophin and cortisone promote retention of sodium and water, but in type 2 nephritis while œdema as a rule increases throughout their administration, diuresis occurs in a proportion of patients when the administration of these hormones is stopped (see p [illegible])

[illegible]

if h [illegible]

estimated along with the blood urea, a urea clearance test carried out and the behaviour of the serum sodium and potassium watched during certain forms of treatment. These observations will have to be repeated at intervals of a week or a fortnight. Daily weighing should be done as a check on the behaviour of the œdema All urine passed must be collected and the amount measured every twenty-four hours. As a rough guide the protein lost in twenty-four hours should be calculated, using Esbach's method along with a knowledge of the volume of urine passed. If the œdema is more than slight the patient should be kept in bed.

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muscularly A reliable method for detection of those sensitive to dextran is not yet available

None of these methods for the control of œdema has yet been proved to abolish the principal mechanism of its formation, the hypoalbuminæmia, and one or other of the procedures described may be needed on numerous occasions throughout the long and tedious course of the disease

Control of Infection.—Patients with long-standing œdema, particularly young children, are very liable to contract infection of the skin, subcutaneous

discretion

When œdema becomes slight or minimal, the patient should be allowed to get up and a sedentary occupation may sometimes be resumed. A check should be made on œdema, blood pressure, blood urea, urea clearance and plasma albumin every month. If œdema increases or an infection develops, the patient should be confined to bed. After many months or years a small proportion recover; but the majority develop the clinical and biochemical picture of chronic type 1 nephritis and require the palliative treatment for that condition. It will be obvious that in some phases of type 2 nephritis patients will be much better looked after in hospital than anywhere else

DIABETIC GLOMERULOSCLEROSIS

(*Kimmelstiel-Wilson Syndrome*)

This syndrome not infrequently occurs in patients with long-standing and usually poorly controlled diabetes mellitus and its features are those of type 2

subacute type 1 nephritis (p 705) Insulin is used when required (see also p. 318).

RENAL AMYLOIDOSIS

Amyloid involving the kidneys was a not very uncommon complication of bronchiectasis, chronic phthisis, chronic osteomyelitis and of chronic sepsis in general, but the more effective treatment of these conditions now available should make it more rare in the future It is also seen occasionally in association with reticulosis, rheumatoid arthritis and myelomatosis Gross proteinuria in any of these diseases should lead to the suspicion of renal amyloidosis. The fully developed clinical picture is that of type 2 nephritis, and diagnosis is difficult because the liver and spleen are frequently not affected, or at least not palpable, and the congo red test is often equivocal. The symptomatic treatment appropriate for type 2 nephritis should be employed (but not corticotrophin or cortisone), together with treatment of the precipitating lesion Progressive failure of renal function leads to death in uræmia if the patient survives the

These remissions last for months, but no claim is yet made that hormone therapy produces cure. Dealing with a small number of patients, mostly adults, the writer has not been impressed with the results, and has observed a condition identical with mild diabetes mellitus develop in an adolescent who gave no family history of that disease. If hypertension or azotæmia is present, hormone therapy should not be used The dose of corticotrophin is 40 units intramuscularly, twice daily in gel form (Armour) for ten days, when it should be withdrawn without tapering off. During the course, procaine penicillin is given daily by intramuscular injection to minimize the risk of intercurrent infection If moonface or the other sequelæ of hormone therapy appear, they can be disregarded as being temporary, but serious electrolyte disturbances may occur in the treatment of type 2 nephritis. At the start, in patients who have been on a salt-poor régime for some time, there may be disproportionate retention of [illegible]

are lost in the urine and hypokalæmia may result. Daily analysis throughout of sodium and potassium is required, as upon the results must depend the course of action to be taken. Hyponatræmia is relieved with the onset of diuresis, which can usually be awaited without change of treatment. Hyperkalæmia is more serious, and the administration of sodium and glucose intravenously increases œdema and is inferior to the promotion of a good flow of urine with dextran if the condition is detected early. It will usually be necessary to stop the corticotrophin at least temporarily. Hypokalæmia calls for oral supplements of potassium (p. 111) Further courses of the steroid hormones may be given, but maintenance doses of cortisone of the order of 50 mg daily by mouth have not prevented recurrence of œdema. The conclusion is that corticotrophin should be tried in a long illness where other forms of treatment have failed, with due regard for the unpredictable consequences which sometimes follow. The first trial of the synthetic hormone, prednisolone, in young children, was followed by a prolonged remission, including disappearance of proteinuria, in four out of five patients It is not yet known whether these patients are cured, but the results warrant further trial. The daily dose used (for young children) was 60 mg. by mouth in divided doses for ten days, followed by 40 mg. for ten days, and so on, the course lasting forty days.

In some patients on a strict salt-poor régime, repeated use of mersalyl with poor results, or tapping may lead to loss of sodium out of proportion to loss of water. The symptoms are weakness, headache, oliguria, azotæmia and, in extreme cases, mental confusion, convulsions and pulmonary œdema. It is particularly in these circumstances when serum sodium is low, and the use of corticotrophin or cortisone therefore undesirable, that a so-called plasma volume expander like dextran is useful. 500 ml. of a 10 per cent. salt-free solution is given intravenously over a period of not less than four hours on four or five consecutive days, depending on the diuresis obtained It was at first thought that dextran was free from side-effects, but it is now known that allergic reactions do occur in some patients though they are very rarely seen in those under a general anæsthetic or suffering from shock. Urticaria, fever, joint pains, nausea and vomiting are usually slight. Respiratory distress is less common. If any of these manifestations develop, the drip should at once be discontinued and 0 5 to 1 0 ml. of 1 : 1,000 adrenaline hydrochloride given intra-

muscularly. A reliable method for detection of those sensitive to dextran is not yet available.

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Control of Infection.—Patients with long-standing œdema, particularly young children, are very liable to contract infection of the skin, subcutaneous tissues, respiratory tract and serous cavities. Pneumonia, empyema, erysipelas [illegible]

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albumin every month. If œdema increases or an infection develops, the patient should be confined to bed. After many months or years a small proportion recover; but the majority develop the clinical and biochemical picture of chronic type 1 nephritis and require the palliative treatment for that condition. It will be obvious that in some phases of type 2 nephritis patients will be much better looked after in hospital than anywhere else.

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underlying disease long enough. Eradication of a septic process, as for example amputation for chronic osteomyelitis, has been claimed to be followed by disappearance of amyloidosis and cure, but the more common experience is that the renal lesion is irreversible by the time œdema appears.

ACUTE RENAL FAILURE : ANURIA

In the past few years much attention has been focused on acute renal failure because the chances of survival have increased so materially, consequent on better management due to a clearer understanding of the processes involved. The causes of the condition may be classified into three major groups as due to oligæmia (pre-renal), to toxic action on renal cells (renal) or to obstruction of the urinary tract (post-renal). In all are found oliguria (less commonly anuria) and

produced

dehydra-

tion. As a result of severe oligæmia lasting about four hours, or a lesser degree lasting for a longer time, patchy necrosis of the tubules is produced, and in

and septic abortion. Severe crushing injuries in civilian casualties are infrequently complicated by anuria, probably because shock is not allowed to persist long enough. *It is more often found in battle casualties. Incompatible blood* transfusion is a well-recognized cause, although hæmolysis *per se* does not cause tubular necrosis, but appears to enhance the effect of moderate shock. Pigment casts containing hæmoglobin or myo-hæmoglobin may be prominent in the lumen of the tubule, but it is not generally accepted that obstruction by them is an important factor in the production of anuria. If oligæmia is the cause, the onset of the syndrome is particularly insidious and is usually suspected only when the urinary output remains low despite the apparently satisfactory management of the factor causing oligæmia.

Toxic Action.—Toxic action directly on the renal cells is exerted mainly on the proximal convoluted tubules. Mercuric chloride and carbon tetrachloride *are examples of this. Hypersensitivity is* thought to be the cause of necrosis of the tubules produced by sulphonamide. In the anuria which occasionally terminates acute type 1 nephritis, the lesion is in the glomeruli and has been held to be due to streptococcal allergen.

Obstruction.—Obstruction, by precipitation *of crystals of sulphonamide* in the renal tubules, the pelves and in the ureters, follows heavy dosage in association with inadequate intake of fluid or excessive loss. Pain in the loins, renal colic and hæmaturia characteristically precede anuria from this cause.

hyperkalæmia is usual. Intercurrent infections are common, particularly in the lungs, and also in the urinary tract because catheter specimens are often required. Possibly in the same category is the hæmorrhagic ulceration which appears on mucous surfaces and is very troublesome to the patient As in chronic renal failure, pericarditis may occur.

Prior to the introduction of modern therapy a very high proportion of these patients died, in many instances because of misguided treatment by forcing

when this begins oliguria is succeeded by polyuria, indicating that while back-diffusion of glomerular filtrate into the blood stream has ceased, the ability to reabsorb properly has not yet returned During this phase along with excessive water loss there is apt to be excessive loss of sodium and potassium also, and less often of calcium.

In prophylaxis it is essential to keep in mind the multifarious causes of anuria and, for example, to guard against it by treatment of shock or hæmorrhage by timely replacement of fluid lost Against the effects of poisonous substances on the renal cells, specific therapy is used at the earliest possible moment, dimercaprol (British Anti-Lewisite) for poisoning with mercuric chloride being an instance.

Oliguria—a volume of urine less than 500 ml in twenty-four hours—is likely to be due to renal failure when the systolic blood pressure is greater than 100 mm Hg. and the *intake of fluid is adequate* Anuria is infrequent, but an output of only a few millilitres of urine per twenty-four hours is common. During the period of oligæmia the scanty urine has a high specific gravity and content of urea, the oliguria of tubular necrosis is characterized by a specific gravity approaching 1010 and a content of 0 5 g per 100 ml or less of urea. The urine contains protein and red blood corpuscles which may undergo hæmolysis and give a reddish-brown tint to the urine. Minor undetected degrees of this syndrome with recovery are probably common enough. Close

the ureters should be catheterized to exclude all possibility of obstruction, and it is probably worth while doing this even if no history of administration of sulphonamide can be obtained Pyelography should not be attempted, as it is dangerous in this condition. For blockage due to crystals of sulphonamide the ureters and pelves are flushed out with a warm 2 per cent. solution of sodium bicarbonate, and if this fails to produce a flow of urine, nephrostomy must be performed and the flushing out done from above. It is also advisable to carry out the régime described in the following paragraphs until urine flow is well established and the biochemical picture is normal, since there is evidence that tubular necrosis may occur along with obstruction.

Obstruction having been excluded, a period of conservative management is begun in the hope and expectation that the renal lesion will heal. The intake of fluid must be restricted to the amount estimated to be that lost by the body in the breath, and by insensible perspiration, against which must be set water derived from oxidation of body fat. The daily requirement is accepted to be about 700 ml. in twenty-four hours. An additional allowance is also made for

fluid lost by vomiting or diarrhœa and, if fever is present, about 100 ml. is added to the intake for each degree Fahrenheit above normal. A warm external

Finally, to the fluid intake is added an amount equal to the volume of urine passed in the previous twenty-four hours, a catheter being used when necessary at the end of each period. Most careful nursing and charting of data are clearly essential. The diet, or rather the source of calories, must be free of protein, to avoid adding to the accumulation of breakdown products of body protein, and also because of its potassium content. It must also be free of minerals because none are being excreted, sodium and potassium being of particular importance. In this connection, fruit juices must be avoided as they contain much potassium. Lastly, the caloric value must be high enough to minimize breakdown of body proteins. All these ends are achieved by the provision of 40 per cent. glucose in 700 ml. of water, giving about 1,100 Cals. per day, which prevents ketosis. In the first instance the glucose may be given by an

and return it in the drip after straining through gauze, but any considerable amount of vomiting demands a change of procedure. Furthermore most patients find the presence of the intra-gastric drip exceedingly irksome, even for a short period In either of these circumstances a Cournand cardiac catheter is inserted into the femoral vein and passed up until the tip is in the inferior vena cava level with the body of the first lumbar vertebra, its position being checked by radiography. The reason for using the inferior vena cava is to permit of the infusion of a highly concentrated solution into a large vessel, thereby

bottle is empty and requires to be changed, and also if it is decided to use a different solution without interrupting the flow. One thousand units of heparin are given in the drip in twenty-four hours to minimize the risk of clotting. Because the treatment may have to be given for several weeks, 100 mg. of ascorbic acid should be added to the drip daily and an adequate amount of vitamin B complex suitable for intravenous use. To each 540 ml. of fluid are

or as some effervescent glucose-containing beverage free of potassium, provided there is no vomiting. Experience with the catheter in the inferior vena cava has proved it to be easily tolerated by the patients who have considerable freedom of movement and, indeed, declare that they are unconscious of its presence.

T ... infection penicillin is the safest antibiotic, and ... daily by intramuscular injection is enou... ...n the urine. If infection develops despite penicillin cover, sulphonamides are contra-indicated and the antibiotic to which the organism is sensitive should be used. The risk of side-effects,

inherent in the use of antibiotics, is increased by the virtual absence of excretion in the urine, but must be accepted to prevent the development of hyperkalæmia due to a severe infection. Chlortetracycline can be given via the caval drip and 250 mg. per day may prove adequate. Preparations of oxytetracycline and tetracycline are available for intramuscular use The course of antibiotic treatment should be as short as possible, and it is advisable to double the amount of vitamin B complex given daily in the drip. If the hæmoglobin falls below 8·0 g. per 100 ml., there is added risk of circulatory failure and also of infection, and a transfusion of packed red cells should be given as slowly as possible to prevent pulmonary œdema, but the high content of potassium should be kept in mind.

It is essential that daily observation be made on the potassium, sodium chloride, urea and carbon dioxide content of the blood Blood glucose estimations

dioxide content of the serum falls below 40 volumes per cent., an ampoule of 40 ml. of molar sodium lactate is added to the glucose drip and, according to the change in the carbon dioxide content, may be repeated daily. It is in order to ignore the level of the blood urea, which rises some 50 mg per day during anuria and continues to do so in the early diuretic stage until tubular function begins to be restored.

It is stated that 25 per cent. of the deaths occur during the healing diuretic phase, and close observation must continue even when the output of urine is increasing daily. When the volume of urine exceeds 1,000 ml per twenty-four hou

hyd

dep

by

porridge or in the drip The fluid intake should not be increased after the output of urine has reached 2,000 ml. per twenty-four hours, provided the blood urea has fallen substantially. The drip is then discontinued and a low protein diet given (p. 720), and when the blood urea is near normal a further increase in protein intake is permitted (p 721) Any non-protein food can be taken freely. When the blood urea is normal, no restriction in diet is required

If there is restlessness not due to a biochemical abnormality which can be corrected, 4 ml. of paraldehyde intramuscularly is the safest sedative. It can be repeated if necessary Acute pulmonary œdema and congestive failure are

oxygen should be given along with 0 5 g of aminophylline given very slowly by

rphine, 15 mg , is injected subcutaneously,

quets to impede venous return (p. 549).

500 ml. of blood may be removed The

red cells may be subsequently returned as a packed cell transfusion given very

[1] Pot cit, Pot acet, Pot bicarb., of each 0 45 g in water to 8 ml., which contains 0·5 g. of potassium, equivalent to about 1 0 g KCl

slowly. Digitalization is best avoided if possible because of the likelihood of vomiting. When congestive cardiac failure is present it may be necessary to use digoxin, and it should be remembered that the amount required, both for control and for maintenance, is less than normal as there is no excretion in the urine Slight hypertension usually develops in the course of the illness, but requires no treatment.

Several methods have been designed to dialyse metabolites from the blood stream, but all are cumbersome; and the most efficient, the so-called artificial kidney, requires a trained team for its operation There is no certain evidence that lives have been saved by its use which would have been lost by efficient employment of the method already described in detail, with the possible exception of the treatment of the marked hyperkalæmia associated with anuria due to severe injuries or war wounds. There is no doubt that renal decapsulation, hypertonic solutions intravenously, caudal analgesia and splanchnic block are of no value. Corticotrophin and cortisone are not helpful and possibly harmful.

The prognosis depends to some extent on the causal factor and is particularly grave when the lesion is glomerular as in acute type 1 nephritis. Over all it is stated that about 70 per cent. recover with the recently evolved conservative [illegible]

those patients who recover, and it is known that renal function as estimated by the concentration test may take many months to return to normal. On the other hand, instances of successful pregnancy subsequent to recovery from acute tubular necrosis are known to have occurred without breakdown in renal function and the general impression is that recovery is eventually complete.

FOCAL NEPHRITIS

Focal nephritis is defined as the appearance of blood, protein and casts in the urine at the height of an infection commonly in the throat. The blood urea, blood pressure and renal function remain normal and œdema is not present. Lodgement of organisms in the kidneys from the site of infection is the cause of the condition, which clears up rapidly when the infection is cured. It is said that cure is permanent.

Some of these cases are, in fact, examples of mild type 1 acute nephritis, and unless a causal organism can be grown from culture of the urine they should be regarded as such In any event, all patients with so-called focal nephritis are best treated as for acute type 1 nephritis, due attention being given to any focus of infection present.

Focal nephritis is to be distinguished from the hæmaturia produced by tiny emboli in subacute bacterial endocarditis. This process does not affect renal function, except rarely when so many glomeruli are destroyed that death results from renal failure. The treatment is that of subacute bacterial endocarditis (see p 572).

FUNCTIONAL OR BENIGN PROTEINURIA

This condition is defined as excretion of protein by the kidneys which is not due to progressive organic renal disease. Its diagnosis is important because the prognosis is excellent, unlike that of latent or chronic type 1 nephritis from which it has to be differentiated; a common problem is the discovery of

proteinuria in a candidate for life insurance, superannuation or National Service. Functional proteinuria is found in various associations, being common after hard physical exercise; it may occur after a cold bath, and it is said to follow *emotional* crises In none of these categories is confusion with nephritis likely. Orthostatic or postural proteinuria occurs in about 5 per cent of older children and adolescents, and as the name indicates, has a relationship to position. Proteinuria is present when the individual is upright, but not when he or she lies down. Lordosis is considered to play an important part, as proteinuria can be provoked by inserting a pillow in the small of the back in the supine position.

Before proteinuria can be considered functional, the following criteria must be satisfied:

1. There must be no history of nephritis. In this connection it must be remembered that latent or chronic type 1 nephritis may develop without a history of an acute attack
2. Hypertension, œdema and other clinical evidence of nephritis must be absent. Here again there is no such evidence in latent nephritis.
3. The urine may contain as much as 2 parts Esbach in the twenty-four hour sample but seldom more, while red blood cells are not seen in the deposit, and only hyaline casts
4. Renal function, as estimated by the concentration test (p 699), must be normal In latent nephritis it is also normal
5. To differentiate orthostatic proteinuria from latent nephritis it is essential to demonstrate that there is no protein in the specimen obtained in the morning before rising from bed. This can be done at the same time as the concentration test Since nephritic proteinuria is often more profuse on assuming the vertical position, it is essential to show that the specimen obtained before rising is quite free of protein.

The importance of diagnosis is twofold. Insurance companies may accept an individual at ordinary rates if albuminuria is shown to be functional, while it is most unfortunate if an erroneous diagnosis of a progressive and eventually fatal disease is made.

No treatment or restriction of any sort is required for functional proteinuria.

TABLE A

Stage 1 Diet for Acute Type 1 Nephritis

		Prot.	NaCl.	Cals.
Daily Ration—		g.	g.	
Milk	10 fl. oz.	9	0 35	170
Unsalted butter or margarine	½ oz.	—	—	110
Sugar	1 oz.	—	—	112
Marmalade or honey	2 oz.	—	—	160
Biscuits	1 oz.	2	0 18	130
Breakfast—				
Porridge (without salt), ½ oz. oatmeal (with milk and sugar from ration)		1·7	0 01	55
Bread, 1½ oz. (with butter and preserve from ration)		3 6	0 46	105
Tea, 7 fl. oz. (with milk and sugar from ration)		—	0·04	—
Dinner—				
Potato, 5 oz., fresh, mashed (with butter from ration)		2	0 02	105
Rice, ½ oz. (made with milk from ration, with preserve)		0 9	—	15
Glucose drink, 7 fl oz.		—	—	164
Tea—				
Bread, 1½ oz. (with butter and preserve from ration)		3 6	0 46	105
Tea, 7 fl oz. (with milk and sugar from ration)		—	0 04	—
Stewed apples, 3½ oz. with glucose, ½ oz		0 6	—	94
Supper—				
Glucose drink, 7 fl. oz.		—	—	164
		23 4	1·56	1489

No salt to be used in cooking and none to be added from the tray. The use of salt-free bread reduces the salt intake to 0 64 g. Total fluid, 38 fl. oz

TABLE B

Stage 2 Diet for Acute Type 1 Nephritis

		Prot	NaCl.	Cals.
Daily Ration—		g	g	
Milk	10 fl. oz.	9	0·35	170
Unsalted butter or margarine	1 oz.	—	—	220
Sugar	1 oz	—	—	112
Preserve	2 oz.	—	—	160
Biscuits	2 oz	4	0·36	260
Breakfast—				
Orange juice		—	—	50
Porridge—½ oz oatmeal (with milk and sugar from ration)		1·7	0·01	55
Bread, 1½ oz. (with butter and preserve from ration)		3·6	0·46	105
Tea, 6 fl. oz. (with milk and sugar from ration)		—	0·03	—
Dinner—				
Meat, 2 oz		14	0·06	140
Vegetables, 3½ oz.		0·3	0·07	40
Potato, 5 oz.		2	0·02	105
Rice or semolina, ½ oz. (made with milk from ration, with sugar or preserve)		0·9	—	15
Water 5 fl. oz.				
Tea—				
Bread or toast, 1½ oz. (with margarine and preserve from ration)		3·6	0·46	105
Stewed fruit, 3½ oz., with glucose, ½ oz.		0·6	—	100
Tea, 6 fl. oz (with milk and sugar from ration)		—	0·03	—
1 egg		7	0·15	80
Supper—				
Glucose drink, 7 fl. oz.		—	—	160
		46·7	2·00	1877

No salt to be used in cooking or to be added from the tray. Total fluids, 39 fl. oz.

TABLE C

Approximate Protein Content of Common Foods

	g. per oz
Egg (1 egg=2 oz.)	3·5
Cheese (except cream cheese)	6-9
Meat, chicken, fish (cooked edible portion)	6-9
Nuts	3-8
White bread, cakes, pastry, buns	2-3
Milk	0·9
Peas, beans and dried figs	1-2
Other fruits and vegetables	<1
Fats	Nil.

Table D

Protein-rich, Salt-poor Diet for Type 2 Nephritis

		Prot. g.	NaCl g.	Cals.
Daily Ration—				
Milk	20 fl. oz.	18	0·7	340
Unsalted butter or margarine	1 oz.	—	—	220
Sugar	1 oz.	—	—	112
Preserve	2 oz.	—	—	160
Breakfast—				
Orange juice, 5 fl. oz.		—	—	50
One egg, or White fish steamed, 2 oz.		7	0·15	70
Bread, 2 oz., salt-free (with butter and preserve from ration)		4·8	salt-free	140
Tea, 7 fl. oz. (with milk and sugar from ration)		—	0·04	—
11 a.m.—				
Milk, 7 fl. oz. (from ration), with Casilan, ½ oz.		13	0·02	52
Dinner—				
Meat, 4 oz.		28	0·12	280
Potato, 4 oz.		1·6	0·16	84
Milk pudding, ½ oz. rice or semolina (made with milk from ration (preserve added) and 1 dessert-spoonful Casilan)		5	0·01	35
Fruit, 7 oz.		1·2	—	78
Tea—				
Fish, 4 oz. herring fried in breadcrumbs		24·8	0·24	260
Bread, 2 oz. (with butter and preserve from ration)		4·8	salt-free	140
Tea, 7 fl. oz. (with milk and sugar from ration)		—	0·04	—
Supper—				
Bread or toast, 2 oz. (with butter and preserve from ration)		4·8	salt-free	140
Milk, 7 fl. oz. (from ration), with Casilan, ½ oz.		13	0·02	52
		126	1·50	2213

No salt to be used *in cooking* and none to be added from the tray. Total fluids, 39 fl. oz.

RENAL CALCULI

The reasons for the formation of renal calculi remain for the most part obscure, but certain factors are recognized as playing a role Small volumes of urine in warm climates, the decalcification of bones which occurs in prolonged immobilization and in hyperparathyroidism, errors of metabolism—gout and cystinuria, and, perhaps most important of all, prolonged infection of the urinary tract The relationship of diet to lithiasis, including imbalance of vitamins and the calcium content of drinking water, is less certain. In the great majority of cases in this country no cause is discovered.

As prophylactic measures a high fluid intake in warm climates and early surgery for hyperparathyroidism are obvious Stones tend to form in the dependent calices of those who are immobilized supine, and in addition to provision of a copious intake of fluid, these patients should have their position changed frequently. Above all, infections of the urinary tract should be dealt with thoroughly, and any cause of urinary stasis searched for and eliminated (p. 726)

Stone in the kidney may give no indication of its presence, even the large staghorn variety, while others cause a dull ache in the loin particularly on movement. Some are detected during investigation of pyuria or of failing renal function. Occasionally the discovery of hypercalcæmia, the result of hyperparathyroidism, may explain the presence of renal calculi (see p. 371). Stones

($\frac{1}{80}$ gr.), is effective in relieving the pain of renal colic Should it persist after fifteen minutes, the dose of morphine should be repeated The course of the stone down the ureter into the bladder should be watched by taking radiographs. The patient should be instructed to drink at least three litres of fluid daily and not to stay in bed, as movement encourages passage of the stone If it reaches the bladder it should also pass through the urethra and all urine should be examined. When recovered the stone should be analysed, and in the hope of minimizing the chance of recurrence certain dietary restrictions may be imposed, depending on the result Oxalate stones call for abstinence from rhubarb, tomatoes, strawberries, spinach, chocolate and strong tea. If a stone is found to be composed of uric acid or urates, the patient should eat no offal and only sparingly of animal protein, though cheese, eggs and milk which contain practically no purine can be eaten freely. The value of these dietetic measures is unproved, and recent work has shown that " pure " calculi are uncommon.

Impaction of a stone in the ureter needs the attention of the urologist to prevent permanent loss of function of the kidney The decision for a consultation is made if the stone remains impacted for a week after the attack of colic and if the intravenous pyelogram then shows either hydronephrosis or no concentration of the dye, indicating impairment of renal function Calculous anuria is commonly the result of impaction of a stone in the ureter when the opposite kidney is not functioning, and here surgical intervention must be immediate. The medical measures described for anuria on p. 714 may be

BACTERIAL INFECTION OF THE KIDNEYS AND URINARY PASSAGES

Bacterial infection may involve the kidneys by the blood stream or ascend by the ureter or spread possibly by way of the lymphatics. A frequent predisposing factor is stasis, produced in the lower part of the urinary tract by prostatic enlargement or neurological disease or by less common lesions such as carcinoma involving the mouths of the ureters. Pregnancy, congenital anomaly and calculus are common causes of stasis in the upper part of the urinary tract which are often associated with unilateral infection. Bilateral pyelonephritis unassociated with stasis is, however, a very common condition, particularly in women.

In more than half the cases the organism is one of the coliform group ... while ... Mixed ... dom if ever confined to the pelvis, and certainly in fatal cases pyelonephritis is found. It may be acute or chronic and is more often than not bilateral

Acute Pyelonephritis.—This may start with a rigor, high fever and backache. *There is frequency of micturition, suprapubic discomfort* and often a burning pain during the act, while the urine may be foul-smelling. A more *insidious onset without much general disturbance is also seen.* Hæmaturia is sometimes present, but œdema and hypertension are not caused by acute infections of the urinary tract To clinch the diagnosis, microscopical examination of the urine must be undertaken, for which purpose a specimen must be obtained by catheter in the female

... bed and given the diet advocated for fevered patients ... full diet is permissible, and since ... lly unnecessary to order any restric- ... ine (or mid-stream specimen in the male) is sent as soon as possible to the bacteriologist, who determines the nature of the organism and its sensitivity to a sulphonamide and to various antibiotics. ... to have the blood urea estimated. While these investigations are ...

cheapness. Sulphadimidine (B P.) is as effective ... dose being 2 g., followed by 1 g six-hourly for seven days Throughout the ... the patient should drink at least three litres of fluid in ...

making the urine alkaline to litmus with sodium bicarbonate in doses large enough and frequent enough for the purpose. Usually 2 g. every four hours is adequate. Alkalinization of the urine is also of therapeutic value in coliform infections because the multiplication of these organisms is slowed down in [illegible]

able, a tetracycline should be given and the patient urged to drink freely.

If the blood urea is found to be raised in a well-hydrated patient and renal function is therefore considered to be abnormal, it is advisable to change the treatment from a sulphonamide to an antibiotic because of the risk of further renal damage. Streptomycin should if possible be avoided in these circumstances because of the increased risk of damage to the eighth nerve due to the slower [illegible]

fæcalis. When using one of the tetracyclines the urine must be kept acid, as they are inert in an alkaline medium Chloramphenicol is useful in addition in some infections with *Proteus vulgaris*. The dose of these antibiotics is 500 mg initially followed by 250 mg every six hours for seven days. It is probably desirable to reserve chloramphenicol for use when no alternative exists in view of the risk of marrow inhibition, slight though it may be Streptomycin is useful in infections with coliform organisms resistant to the sulphonamides, [illegible]

with *Proteus vulgaris* or *Pseudomonas pyocyanea* is particularly difficult to eradicate, and a combination such as streptomycin and sulphadimidine is likely to be more successful than either alone Nitrofurantoin is sometimes successful in infection with *Proteus vulgaris* when other forms of treatment have failed. [illegible]

the ex[illegible]
choice [illegible]
side-ef[illegible]
approp[illegible]

are usually the most expensive. The older urinary "antiseptics" such as pyridium, hexamine, hexyl-resorcinol and mandelic acid are now seldom if ever used as they are much less efficient than sulphonamides and antibiotics.

Preferably when treatment has taken effect and toxic manifestations have [illegible]

nephrosis is found or renal anomaly or calculus, the advice of the urologist should be obtained, and in many instances cystoscopy and retrograde pyelography will be required to obtain complete information. In such cases sterilization of the urinary tract may not be achieved with the appropriate medical treatment, or at best relapse will occur a short time afterwards and surgical measures should therefore be carried out if the functional capacity of the other kidney permits.

In pregnancy some dilatation of both ureters is very common, but compression of the ureter by the fœtal head against the pelvic brim is often the factor causing stasis and infection. Obstruction ceases after delivery, and drainage of the ureter by catheterization is now seldom required with the advent of sulphonamides and antibiotics; but the onus on the doctor still remains to make quite certain that infection does not persist after delivery, since it is thought that chronic pyelonephritis causing renal failure in later life may often be a legacy of pregnancy.

The prognosis of acute pyelonephritis is little influenced by the severity of [illegible] but depends rather on the resistance of the organisms and

[illegible]
and samples should be sent to the bacteriologist at the conclusion of treatment, four days later and two months later. It cannot be too strongly emphasized that search for an underlying factor leading to stasis and predisposing to infection should be made in every patient, and even in all apparently straightforward cases without a factor causing stasis, cultures of the urine should invariably be made after treatment is concluded.

Cystitis seldom occurs alone unless there is obstruction below the bladder or injury to its mucosa, as for example by enlarged prostate or calculus respectively. It is usually associated with infection higher in the urinary tract, in which case the treatment is the same as for pyelonephritis.

Chronic Pyelonephritis.—This may be bilateral or unilateral. One form of presentation is persistent pyuria with backache and bouts of fever and frequency of micturition. With bilateral involvement gradual deterioration of renal function ensues, usually over a period of years with ultimate death from uræmia. Investigation and treatment are on the same lines as for acute pyelonephritis In chronic pyuria, tuberculous infection must be excluded with particular care by bacteriological examination of a twenty-four-hour specimen of urine and if necessary cystoscopy. The results of chemotherapy are likely to be less satisfactory in chronic cases, but surgery may effect a cure when the [illegible] function of
lesion is unilateral, for exam[illegible]
the other kidney is normal. [illegible]
lower bowel or female genit[illegible]
cause of pyuria or even obstruction and pyonephrosis.

Another form of presentation is that of chronic renal insufficiency, and it is generally accepted that death from uræmia occurs as frequently from chronic

urinary infection the diagnosis is often made by the pathologist With better treatment of the infection in the acute stage it is probable that fewer illnesses of this type would occur.

Since infection is no longer present, the treatment is that of chronic renal failure as outlined on p. 708. Because the pathological changes of chronic pyelonephritis may involve the tubules to a greater extent than the glomeruli, syndromes dependent on interference with tubular reabsorption are occasionally superimposed on chronic renal failure Loss of sodium in the urine is not

anorexia, vomiting and drowsiness are prominent, and a fall of blood pressure

wea
pot
and
by
exc.

the urinary output exceeds one litre per twenty-four hours if it is intended to

therefore important, particularly in patients under forty-five, and in those in the early malignant phase of hypertension, not to consider raised blood pressure as "essential" without a full investigation, since occasionally nephrectomy may result in the removal of the source of humoral pressor substances If tests of combined function (p. 699) give normal results, intravenous pyelography should be done, and repeated if a unilateral abnormality is apparently present, since it is recognized that a normal kidney for unknown reason occasionally fails to concentrate diodone It should be remembered that the whole kidney

distortion of the
the urologist of
catheterization.

Nephrectomy is carried out only if the presumed normal kidney shows normal function In only a minority of patients is there a substantial reduction in blood pressure after nephrectomy, and even fewer are cured. Failure is presumably due to undetected pyelonephritis involving the other kidney, to the malignant phase having already damaged the other kidney, or to the hypertension being in fact "essential" Nevertheless, striking successes have been occasionally obtained by nephrectomy.

RENAL CARBUNCLE: PERINEPHRIC ABSCESS

These conditions arise from an infection of the blood stream with staphylococci complicating boils or other lesions of skin or bone. One or more abscesses form in the renal cortex; healing may then occur or there may be rupture into the perirenal tissue, or, much less commonly, into the *renal pelvis*. Before the discovery of antibiotics, treatment of perirenal abscess was entirely surgical, but there is now some slight chance of cure with an antibiotic to which the organism is sensitive. Pus and organisms are not usually present in the urine, and therefore if the original focus is healed, or deep-seated, sensitivity tests cannot be made. The effect of treatment can then be judged only by the clinical condition, the temperature chart and leucocyte count. Penicillin should be tried first in a dose of at least 250,000 units by four-hourly intramuscular injection. If there is no favourable response in forty-eight hours, erythromycin, 2 g. daily, should be tried. Even with the vigorous use of antibiotics, most cases will require surgical drainage.

NEPHROPTOSIS

This is a condition of undue mobility, usually of the right kidney, which is

be provided to maintain the kidney in position.

J. B. RENNIE

CHRONIC RHEUMATIC DISEASES

INTRODUCTION

THE RHEUMATIC DISEASES, both acute and chronic, are, for the most part, diseases of temperate climates. In countries enjoying this mixed blessing they constitute a serious menace to the health and well-being of the community. Only within recent years have statistics been compiled which indicate the magnitude of the problem. It is officially admitted that one-sixth of the total annual invalidity of insured persons in Great Britain is due to rheumatic disease in one or other of its forms. In Scotland, with a population of approximately 5 million, 50,000 insured persons are totally incapacitated annually for an average period of sixty days. Investigations carried out by the writers indicate that at least 300,000 new cases of rheumatic [illegible] entailed.

When the section on treatment has been studied, it will become clear that many of the complex and specialized measures required for diagnosis and treatment are outside the scope of general medical practice, and it is officially admitted that there is an urgent need for an increase in the facilities for the treatment of the more chronic forms of rheumatic disease. It is for these reasons that we have advocated most strongly the establishment of a national scheme for the control and treatment of the chronic rheumatic diseases, the essential feature of which would be the provision in selected areas throughout the country of clinics in charge of physicians who have received special post-graduate training, and who would decide whether patients suffering from chronic rheumatic disease should be treated by the family physician at home, at the [illegible]

[illegible] more severe forms, and by the immediate institution of the proper lines of treatment, can the regrettably common legacy of permanent incapacity be reduced or avoided.

Before any scheme of treatment is adopted for an individual patient, it must again be emphasized that accurate diagnosis of the type of rheumatic disease present is vitally important. To label a disease "rheumatism" and to prescribe analgesics is no longer justifiable in view of the great advances in treatment [illegible] been reac[illegible] process, [illegible] the diseas[illegible] chronic st[illegible]

processes is essential if treatment is to be applied in a rational manner. The measures adopted during the acute or active phase differ radically from those employed in the subacute or chronic state, and the use of over-strenuous measures at the wrong time may lead to disaster. To estimate the de... f

sedimentation rate of the red blood cells should be carried out in every case of arthritis. The technique of this test is simple and should be undertaken by every family doctor who wishes to treat the more severe forms of chronic rheumatic disease. Accordingly the technique of the test is described on p. 777 and its diagnostic and prognostic value is discussed.

When the physician has reached a correct diagnosis and has assessed the degree of activity present, the next st

treatment, is to institute a thorough

Expert opinion is essential before the

have his tonsils removed or his sinuses drained, to mention one or two examples, but not infrequently the role of the practitioner will be to protect his patient from the over-enthusiasm of the specialist

Many factors are believed to play a part in the ætiology of the different forms of chronic rheumatic disease—infection, environment, constitution, occupation, the anatomic type of the patient, impairment of the body mechanics, etc. In a particular case one factor may appear to dominate the picture. The physician should remember that a healthy body has, until its vitality is impaired, a remarkable capacity for withstanding isolated insults offered to it by its environment externally and its owner internally. Accordingly, although the amelioration of pain is the first consideration both of the patient and his physician, the latter will not have fulfilled his obligations until he has made an effort to discover and to deal with factors which may be detrimental to the general health of the patient, or which may be exercising an adverse effect on his disease.

The first consideration in the treatment of chronic rheumatic disease is to secure the co-operation of the patient. Chronicity is an essential feature of ... full confidence

methods which have been carefully though...

... principles underlying correct treat-

nt.

ic

rheumatic disease is far from being as gloomy as has been formerly held by the laity and the profession. A return to the enjoyment of useful citizenship can be attained in a surprisingly high proportion of cases

There are three fundamental principles which govern the treatment of all forms of chronic rheumatic disease:

1. The improvement of the general health of the patient
2. The elimination or correction of ætiological factors.
3. Treatment of the local manifestation of the disease.

CLASSIFICATION

It has been thought advisable to adopt as simple a classification as possible, using the nomenclature in common use among general practitioners rather than the more recent terminology based on ætiological concepts over which opinion is still sharply divided. From the point of view of treatment, the chronic rheumatic diseases can be divided into three main groups :

1. Rheumatoid arthritis and ankylosing spondylitis.
2. Osteoarthritis
3. Non-articular rheumatic diseases

Osgood has given an excellent definition and comparative classification of the [illegible] which we quote verbatim :

[illegible] mmon

[illegible]

fever but presents a somewhat similar articular picture (in the British Isles this *is the synonym most commonly employed*), '*Atrophic*' *because very early in* its course we may appreciate characteristic atrophy (halisteresis) or erosion of bone structure and soon accompanying atrophy of the musculature, 'Proliferative' because Nichols and Richardson (1909) showed that an early change, perhaps the very earliest, is a proliferation of the synovial membrane of the affected joints, which becomes thickened (pannus) with the formation of synovial tabs or villi; 'Ankylosing' because, in an unchecked disease, the joints may eventually become ankylosed, at first by fibrous adhesions and later by true bony fusion. In this first great type we include Still's disease in children and, at least for the present, the 'Marie-Strumpell' syndrome, or 'spondylose rhizomélique', *the main ankylosing lesions of which usually appear first in the* sacro-iliac joints and spine The so-called root joints, i e the shoulders and hips, frequently are also affected."

Osgood's definition of group 2 is as follows :

"The second great type, in which there is no striking difference in sex [illegible] frequently, and in [illegible] ge of forty years, [illegible] or *degenerative* [illegible] rosis) (the usual British term) because the bony changes are evident early in the disease; 'Hypertrophic' for the same reason, the articular bone-end changes representing [illegible] of chondro-osseous spicules or ridges ;

[illegible]

of an unchecked disease. One spinal exostosis or spur may fuse with an impinging spur, but the articular bone ends, even after the degenerated cartilage has been completely absorbed, become eburnated (often actually polished), but do not fuse"—"A Survey of Chronic Rheumatic Diseases", pp. 227-78 Oxford University Press, 1938.

We have followed the committee appointed by the British Medical Associa...

1. Acute or subacute rheumatic fever.
2. Specific infections: Gonococcal, dysenteric, tuberculous, syphilitic, pyogenic.
3. Metabolic and blood diseases: Gout, hæmophilia.
4. Organic nervous disease: Charcot's joints in tabes and syringomyelia.

The reader is referred to the appropriate sections for the treatment of the primary condition in this group, while the general principles enunciated in the section on *chronic rheumatic diseases are in general applicable to the joint* manifestations.

PROPHYLAXIS OF THE CHRONIC RHEUMATIC DISEASES

Rheumatoid Arthritis.—Recent surveys of the incidence of rheumatoid arthritis in the general population reveal no evidence that the disease affects one social class more than another, or that the type of employment is of ætiological importance. The impression that thin, visceroptotic people are more prone to develop rheumatoid arthritis than those of sturdier build is probably *erroneous. Research has not as yet shed any light on the ætiology of the disease.* In these circumstances it is not possible to recommend any specific measure to reduce the general incidence or to prevent the onset of the disease in the individual.

Osteoarthritis.—Osteoarthritis is more an arthrosis than an arthritis, being a degenerative condition and an accompaniment of the ageing process. It is ... tional defect in the patient's

incidence of arteriosclerosis and hyper... high

fractured, a secondary osteoarthritis will result in adjacent joints unless proper alignment of the fragments is procured. *When a fall or injury results in trauma of the joint structures and contusion of the overlying tissues, proper* treatment by rest followed by heat, massage and movement may delay and minimize the effect of the trauma in conditioning the occurrence of osteoarthritis. Long-continued trauma from occupational strains is a common cause of osteoarthritis. ... arthritis in particular sites. ... of the wrist, elbo... hips are more usually affected. The question arises, when early signs of osteoarthritis are noted by the doctor, whether a change of occupation should be advised before the affected joints become *hopelessly crippled.* The decision in such a case will depend on the circumstances, but the advice to change one's *occupation in middle* age can seldom be taken for economic reasons

More hopeful fields for the reduction of osteoarthritis in industry lie in the province of public health administration Improvement of working conditions in factories, workshops, mines, etc., would go far to lower the incidence of this disease

Another factor which leads to continuous joint strain and undue pressure on the articular surfaces is obesity. Its correction by dietetic restriction (discussed on p. 324) is a preventive measure of great importance

Postural defects predispose to the development of osteoarthritis for the same reason as does obesity, and their correction by special exercises or orthopædic measures is important in its prevention The commonest faults are lumbar lordosis and scoliosis, genu varum or valgum, and pes planus.

There is no evidence to suggest that focal sepsis is of ætiological importance in osteoarthritis.

RHEUMATOID ARTHRITIS

The treatment of rheumatoid arthritis is governed by the stage of the disease and the degree of activity present when the patient is first seen by the medical practitioner We have arbitrarily divided the disease into three stages, although in practice no sharp dividing line exists.

THE ACUTE STAGE OF RHEUMATOID ARTHRITIS

In order that the objects of treatment may be better understood, a brief description of the main clinical features of a classical case of rheumatoid arthritis in the acute stage will be given Although the locomotor symptoms are predominant, there is also general constitutional disturbance The patient complains of lassitude even when at rest and of excessive fatigue on the slightest effort. There has been a progressive loss of weight and the appetite is poor. The extremities are cold and clammy, and the body sweat may have a peculiarly rank odour. A mild fever ranging from 99° to 101° F. may be present. Blood examination shows a moderate degree of hypochromic anæmia, often a slight polymorphonuclear leucocytosis and a marked increase in the sedimentation rate of the red blood corpuscles. Many joints are swollen and painful, the small joints of the hands and feet usually being the first to be affected. The lesions are mainly peri-articular at this stage, only rarefaction of the bone ends being seen on radiological examination Muscular wasting is an early and prominent feature of the disease The treatment of such a patient embodies two fundamental principles .

1. General treatment which includes measures (*a*) to improve the patient's general health and (*b*) to eradicate or correct ætiological factors
2. Local treatment of the joints

General Treatment.—The principles governing the treatment of a chronic infective disease such as tuberculosis are likewise of fundamental importance in rheumatoid arthritis and must be observed with scrupulous attention to detail if the best results are to be obtained It cannot be too strongly emphasized that treatment embraces the management of the patient as well as measures which aim at relieving the disease.

As already stated, the *psychological aspect* is of particular importance in all diseases which tend to run a prolonged course. Accordingly the physician

by aspirin alone, compound tablets of codeine (B.P.), one or two tablets twice or thrice daily, should be prescribed in addition. The use of more powerful analgesics such as morphine should be avoided if possible on account of the danger of addiction. A drug of the barbiturate group, such as amylobarbitone 0.1 to 0.2 g. ($1\frac{1}{2}$ to 3 gr.), should be used if sleep is disturbed. If the patient is anæmic, iron should be given, but its administration by mouth is seldom effective in active rheumatoid arthritis. Preparations are now available which can be injected intramuscularly or intravenously (p. 406). A total of 1 to 2 g. constitutes a course. Improvement in the anæmia follows in a significant proportion of patients. Liver extracts and cyanocobalamin are of no value except on the rare occasions when megaloblastic anæmia and rheumatoid arthritis coexist. Additional calcium is not required if the patient is encouraged to drink plenty of milk. Provided the diet is well balanced and adequate in amount, the addition of synthetic vitamins will not be necessary (p. 742). Claims regarding the favourable effects of large doses of vitamin D (100,000 to 300,000 units daily) have not been confirmed. There is seldom any indication for the prescription of thyroid extract or sex hormones. Cinchophen and colchicine are contra-indicated in rheumatoid arthritis, since there is no evidence of derangement of uric acid metabolism. Neostigmine has been used for the relief of muscular spasm, but the initial claims made have not been substantiated. Its use is not recommended. Clinical trials have shown that no beneficial effects have followed the use of antibiotics such as penicillin and the sulphonamide drugs.

Of the multitude of drugs used empirically, mention may be made of arsenic, iodine, sulphur, guaiacol, ortho-iodoxybenzoic acid, histamine, bee venom, [illegible]

is no proof of their value and they are no substitute for a carefully considered and comprehensive plan of treatment.

There are three drugs which require special consideration, namely phenylbutazone, gold and cortisone.

Phenylbutazone (*Butazolidin*).—This drug, a pyrazol derivative, was first used in the treatment of rheumatoid arthritis in 1951. It is a powerful analgesic, capable of relieving pain in a high proportion of cases. It was thought at first that the drug had a specific effect and could cause a reduction in the activity of the disease. This impression has not been substantiated by subsequent observations. [illegible] treatment, joint swelling [illegible] the drug

Patients may [illegible] this proves inadequate, the amount may be increased by 0.1 g. daily to a maximum of 0.6 g. If adequate subjective improvement has not occurred after three or four days on this dose, the drug should not be continued, as the incidence of toxic effects increases sharply above this level.

Toxic effects occur in 40 to 50 [illegible] during the first few weeks of treatment. [illegible] stomatitis, dyspepsia, nausea and [illegible] skin rashes and albuminuria are the most frequent. More serious, though much rarer complications, are hæmorrhage or perforation of peptic ulcers, jaundice, agranulocytosis, aplastic anæmia, thrombocytopenia, optic neuritis and toxic

psychosis Deaths have been reported, mainly as a result of toxic effects on the bone marrow. Elderly people, especially females, appear more liable to side-effects. The drug should not be given in the presence of cardiovascular, renal or hepatic disease, or to patients with a history suggestive of peptic ulcer. Salt restriction is recommended to minimize the sodium-retaining effect of the drug. This drug has been widely used in the treatment of rheumatoid arthritis It is a powerful analgesic, but in view of its potential toxicity and the absence of any true anti-rheumatoic effect, its administration over a prolonged period in a chronic disease such as rheumatoid arthritis cannot be given unqualified approval. The simpler and safer analgesics already discussed will prove adequate in the majority of patients if they are combined with effective local treatment of the painful joints.

Chrysotherapy.—Gold was first used in the treatment of rheumatoid arthritis as a result of the belief in its value in the treatment of pulmonary tuberculosis. Although the conception that direct infection with living organisms is the cause of rheumatoid arthritis has largely been discarded, gold continues to be used in its treatment Its mode of action is unknown The lack of any immediate dramatic response, the undoubted psychological value of a weekly injection combined with regular supervision, and the fact that between 50 and 60 per cent. of patients improve on a conservative regimen of treatment, have made it very difficult to reach a definite conclusion as to the value of chrysotherapy. Nevertheless, a review of the literature reveals that many authorities still believe that benefit follows its use in a worth-while proportion of cases (50 to 70 per cent). It is generally accepted that in those patients who respond, the first course of gold is the most effective, the results of subsequent courses are often disappointing Satisfactory remissions following its use occur more frequently in early cases, but this could be truthfully said about all forms of treatment. Chrysotherapy should only be considered after a conservative regimen of treatment has been given a thorough trial and has failed to control the progress of the disease In spite of its limitations, interest in the use of gold has been renewed since it has been shown that prolonged treatment with cortisone frequently proves impracticable (p. 739)

It should be clearly recognized that the exhibition of gold salts must be considered merely a part of and not a substitute for a general plan of treatment carefully arranged for each particular patient The oil-soluble and water-soluble salts are equally effective, provided the dosage of gold is the same. Since the water-soluble preparations are cleaner and easier to handle, they are to be preferred Myocrisin, a 50 per cent solution of sodium aurothiomalate in water, is a proprietary preparation widely employed Preparations of colloidal gold are not recommended. Following the injection of gold salts the level of gold in the plasma rapidly rises and gold is thereafter deposited in every cell in the body The highest concentration is found in the liver, kidneys and skin, sites which clinical experience has shown to be chiefly affected by toxic reactions. Another point of clinical interest is that gold is present in the synovial membrane in higher concentration than in muscle and that the gold content of the synovial membranes of arthritic joints is much higher than that of the synovial membranes of normal joints. Excretion is largely by the kidneys, but a marked retention occurs in the body when the usual weekly dose of 0 1 g of gold salt is given. At least 80 per cent is retained and consequently the excretion of gold can be demonstrated in the urine for many months after treatment has ceased.

The fate of gold in the body is of great clinical interest as it explains some of the dangers of [illegible]
by toxic reactions, [illegible]
than is usually p[illegible]
reactions can be reduced in frequency and severity and the number of patients who will be enabled to continue treatment will be increased. The course of chrysotherapy generally recommended consists of twelve intramuscular injections at weekly [illegible]
100 mg. [illegible]
that equa[illegible]
giving th[illegible]
injected at [illegible] to a maximum of 50 mg. of gold salt. Thereafter the course may be repeated for a second, third or fourth time, depending on the clinical response and the absence of reactions. Chrysotherapy should be discontinued for at least eight weeks between courses. Others have stated that better results are obtained if the effects of the first course of treatment with 1 g. of gold are maintained by a monthly injection of 50 mg. for periods up to a year, but there is no clear proof of this and there is a risk that unnecessarily large amounts of gold may be given.

[illegible]

preventing their onset and no way of recognizing those patients in whom toxic effects will occur. Hence it is advisable for the physician to explain the dangers to the patient or his relatives before beginning treatment. Gold treatment [illegible]

[illegible]

counts has been exaggerated ; their usefulness is limited as agranulocytosis may appear abruptly within two or three days of the count being found normal. In many clinics, when leucotoxic drugs (gold, arsenic, thiouracil) are used, routine white cell counts have been abandoned in favour of careful instructions to the patients to report to their doctor immediately any symptoms of general ill-health, fever, or sore throat develop. General skin reactions, purpura, marked leucopenia, jaundice, albumen, casts and blood in the urine are findings of [illegible]

[illegible] and then to begin with only in reduced dosage. A recurrence of toxic [illegible]

but indicates the need for careful urine analysis prior to each subsequent dose of gold. Reference should be made to the appropriate sections for the treatment of the various toxic manifestations should they arise. Until the introduction of dimercaprol (B.P.) (British Anti-Lewisite, BAL) in 1946, treatment was purely symptomatic. This drug, originally designed for the treatment of arsenical poisoning, has been used with gratifying results for the treatment of

various toxic manifestations arising from gold therapy. The drug combines with most heavy metals to form a stable compound which is excreted in the urine. For all forms of severe toxic reactions, dimercaprol is given in doses of 3 mg per kilogram of body-weight every six hours for three or four days. The calculated quantity is injected intramuscularly. Smaller doses will be found effective for less severe toxic reactions. In gold hepatitis the dose should never exceed 3 mg per kilogram of body-weight given at six-hourly intervals and should generally be less, since it has been shown that in cases with liver damage the toxic effects from dimercaprol may be severe. Gold has been used in combination with cortisone in the hope that the initial improvement on cortisone could be consolidated and maintained, but results have not been encouraging. The simultaneous administration of two toxic drugs such as gold salts and phenylbutazone should be avoided.

In conclusion, we feel it cannot be denied that the use of gold salts in the treatment of rheumatoid arthritis is unsatisfactory in view of the incidence of toxic reactions and the fact that a substantial proportion of patients derive no benefit from their administration. The circumstances which may justify the use of this drug have been discussed and the dangers and limitations of chrysotherapy have been stressed.

Cortisone.—The results of the administration of cortisone to patients suffering from rheumatoid arthritis and rheumatic fever were reported by Hench and his colleagues in the Mayo Clinic in 1949. The hormone was administered by intramuscular injection in doses of 200 to 300 mg for two or three days and thereafter 100 mg daily. Cortisone acts equally well when given by mouth in the form of tablets. Oral dosage is similar or only slightly greater than parenteral dosage. Within a few days of the commencement of treatment, pain and swelling in the affected joints begin to subside and stiffness is markedly diminished. In two or three weeks pain has largely disappeared and patients previously severely incapacitated are able to resume normal activity. The blood sedimentation rate falls, anæmia improves and a marked improvement occurs in mental outlook, amounting to euphoria in some cases. Continued administration of the hormone in the dosage required to control the clinical features for several weeks or months produces a number of side-effects. In 50 per cent of cases on long-term continuous treatment one or more of the following have been noted: disturbance of the electrolyte balance leading to retention of salt and water and loss of potassium, hypertension, rounding of the face, increased growth of hair, acne, striæ, glycosuria, voracious appetite, obesity, nervousness, insomnia and undue fatigue. These undesirable effects are usually readily reversible on withdrawal of cortisone. Much has been learned during the last five years about the use of cortisone in rheumatoid arthritis and it is now possible to express a more definite view on its place in treatment. It has become abundantly clear that improvement in function results from a partial suppression of the inflammatory reaction in connective tissue. This effect is in no way specific. The disease process is not checked, as evidenced by progressive increase in the radiological evidence of joint damage in patients rendered free from all symptoms by cortisone. Experience with patients maintained on cortisone for as long as three years does not suggest that the natural course of the disease is significantly altered by such continuous suppression of symptoms. With regard to dosage, it is generally agreed that if the maintenance dose exceeds 100 mg. daily sooner or later troublesome side-effects will develop. These are discussed in detail on

p. 85. Experience has also shown that in any group of patients under prolonged treatment, cortisone will have to be withdrawn in a substantial number because of the development of intolerable side-effects, the occurrence of one of the complications discussed above, or because the therapeutic response does not justify a continuance of the hormone. On cessation of cortisone therapy symptoms of arthritis reappear in the great majority of cases and may become more severe. In addition, what has come to be described as the cortisone withdrawal syndrome may develop. Symptoms may appear within a few days or be delayed for a week or two.

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suppression, as they persist after adrenal function has returned to a normal level. If cortisone has to be withdrawn, it should be done very slowly over a matter of two or three weeks, in the hope that endocrine equilibrium will be regained before treatment is terminated.

A controlled clinical trial designed to compare the value of aspirin and cortisone in the treatment of early cases of rheumatoid arthritis (duration 3 to 9 months) has been conducted in a number of centres in Great Britain under the

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aspirin and those on cortisone It was concluded that for practical purposes

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l1 before treatment with aspirin or

cortisone was started. At the end of one year, statistical analysis of the results again showed no significant difference between the two groups of patients. It would appear, therefore, that cortisone should rarely be used in the long-term treatment of rheumatoid arthritis. A number of authorities, both in this country and America, do not subscribe to this view. They maintain that, although in the majority of cases of rheumatoid arthritis, the disease can be controlled by such basic measures as rest, adequate splinting, physiotherapy and salicylates, a minority continue to run a progressive course. In such patients it is claimed that the prescription of cortisone (or corticotrophin) when combined with a sound basic regimen may lead to the restoration of useful function when permanent crippledom seemed otherwise inevitable. It is difficult to assess the validity of this view or the frequency with which this type of case is encountered In our experience they are rare, but others claim that between 10 and 15 per cent. of cases fall into this category. If a decision to use cortisone is made, it must be explained to the patient that the hormone has no curative effect and its administration will have to be continued for a long period, perhaps indefinitely. This implies continuous and close supervision. It must also be borne in mind that complications become more common with increasing age and prolonged treatment.

It is now considered wise to avoid high doses initially. A dose of 75 mg. daily is given for one week. If adequate suppression is achieved, the dose is gradually reduced by 12 5 mg. ($\frac{1}{2}$ tablet) every two to three days until a slight increase in symptoms occurs. This should be regarded as the maintenance dose. Adjustments will be required from time to time If a useful degree of

relief is not attained in a week on 75 mg. daily, the dose may be increased by 12·5 mg. If this should still prove inadequate, it is advisable to withdraw the drug slowly. Patients given 100 mg. daily for any length of time will inevitably develop signs of hyperadrenalism and serious complications become more frequent. With the doses recommended, marked disturbance of the electrolytes is unusual, but should signs of sodium retention, in the shape of rapid gain in weight or œdema, appear, salt in the diet should be restricted and potassium chloride, 2 to 3 g., given daily. Mercurial diuretics will seldom be required, but may be used if œdema persists. A troublesome feature of long-term treatment, especially in women, is increasing obesity. This is particularly undesirable if weight-bearing joints are affected and must be controlled by appropriate dietetic restriction. Blood pressure must be recorded at regular intervals in view of the insidious development of hypertension in a proportion of patients.

It was hoped that cortisone might prove a useful adjunct when deformities had to be corrected by manipulation or operation. Experience in Great Britain in this field has been disappointing. Cortisone has proved little if any more effective than analgesics such as aspirin and codeine. In America orthopædic surgeons have reported cortisone to be helpful in pre- and post-operative procedures designed to restore or increase function in damaged joints. It would appear reasonable to expect such an effect, but further experience is required to show that equally satisfactory results cannot be achieved with aspirin and codeine.

A further use for cortisone may be in the control of a severe exacerbation of activity with rapid development of deformities which cannot be prevented by conservative measures. In these circumstances the moderate doses recommended for maintenance may prove inadequate. Doses as high as 150 to 200 mg. daily may be needed for two to three weeks in these rather rare cases. As soon as reasonable suppression has been attained, the dose of cortisone should steadily be reduced and finally the drug should be withdrawn. On cessation of cortisone therapy the position must be consolidated by fixation of the more severely affected joints in plaster splints, combined with the prescription of maximum doses of aspirin supplemented by codeine, and in selected cases the intra-articular injection of hydrocortisone. With joints held in good alignment and local symptoms at least partially controlled by the above measures, it may be possible to prevent further deterioration when the inevitable recurrence of disease activity takes place on withdrawal of the hormone.

Hydrocortisone.—Hydrocortisone has been shown to have a similar anti-inflammatory action in rheumatoid arthritis when given by mouth. Hydrocortisone acetate is rather less effective, weight for weight, than cortisone acetate, but hydrocortisone free alcohol is rather more potent. Both forms have been submitted to clinical trial and no advantage over cortisone has been found. Side-effects and complications are similar. Hydrocortisone acetate in suspension is the preparation of choice for intra-articular use (see p. 745).

Prednisone and Prednisolone (*Metacortandracin and Metacortandrolone*).—Two new steroids, analogues of cortisone (Δ^1-cortisone) and hydrocortisone (Δ^1-hydrocortisone), now known as prednisone and prednisolone, have been shown to be about four times as potent weight for weight in suppressing signs of inflammation as the two older steroids. Doses ranging from 5 to 25 mg. daily have proved effective in controlling symptoms in the majority of patients. Preliminary reports state that the increased potency of these new steroids is not

accompanied by a rise in the frequency or severity of side-effects. It has also been claimed that a number of patients who had shown little or no improvement on cortisone or hydrocortisone responded remarkably well to relatively small doses Perhaps the most significant observation recorded to date is the absence of significant effects on electrolytes. This may be important in circumstances where sodium retention and potassium loss prove a serious obstacle to continued treatment. Unfortunately, no such dissociation between the power to suppress inflammation and other hormonal effects has been demonstrated. Signs of hyperadrenalism appear in the majority of patients requiring a daily dose of 20 mg. or over for more than two to three weeks. The most serious complication has been the occurrence of peptic ulceration, which appears more commonly than with cortisone or corticotrophin. It remains to be seen whether they will prove of greater value than cortisone or hydrocortisone in the treatment of rheumatoid arthritis. There now seems to be a real possibility that by further modifications of the steroid nucleus compounds may be produced which are free from unwanted hormonal effects and hence more suitable for the long-term treatment of rheumatoid arthritis.

Corticotrophin (ACTH)—The dose of this hormone required to produce adequate clinical suppression of symptoms in rheumatoid arthritis varies The initial dose of corticotrophin gel recommended is 40 international units every twenty-four hours. If response is satisfactory, the dose is slowly reduced by 5 units every two to three days until the maintenance level is found. Side- [illegible]

[illegible] restricted the use of corticotrophin in rheumatoid arthritis. It has been noted, however, by a few workers that sustained remissions of the disease have followed the use of corticotrophin over a period of months. This is in contrast to the almost invariable recurrence of symptoms which rapidly follows the withdrawal of cortisone It may be that the greater advantage to both patient and doctor of giving cortisone orally has led to a premature loss of interest in the use of corticotrophin.

Vaccines.—While it is universally accepted that vaccines can produce valuable effects in the prevention of certain diseases due to known infective agents, it is highly debatable whether they are of any value as curative agents in established disease. It is, therefore, not surprising that considerable scepticism exists in regard to their therapeutic value in rheumatoid arthritis, a disease whose ætiology is unknown and which may not be due to a bacterial infection at all It might be thought that since many thousands of cases of rheumatoid arthritis have been treated with vaccines during the past twenty-five years indisputable proof of their efficacy would have been produced by those who advocate their employment. Unfortunately this is not the case. Reiterated claims that clinical benefit is produced in a certain proportion of cases are no substitute for statistical data obtained from a properly controlled experiment which should demonstrate a significantly higher proportion of good results in cases treated with vaccines compared with a control series receiving injections of sterile saline. The need for properly controlled research in this field is urgent. While the therapeutic value of vaccines is at least debatable, it is universally agreed they are *potentially dangerous* if employed injudiciously in the acute stage of the disease or in excessive doses At the time of writing the majority

of physicians believe that vaccines are of no value and accordingly their employment is not recommended.

The one undoubted benefit which the weekly injection of any substance including vaccines has to offer is that it enables the physician to see his patient at regular intervals and gives him the opportunity of reviewing the progress of the case and of making adjustments to the therapeutic programme when necessary.

Non-specific Protein and Fever Therapy.—The parenteral injection of foreign protein, e g boiled milk, peptone, TAB vaccine and the raising of the body temperature by the use of hot baths and packs, hot-air cabinets or short-wave machines are forms of treatment employed much less frequently than twenty years ago. This suggests that the original claims were undoubtedly exaggerated

Certain of the observations in regard to vaccine therapy and its dangers are equally applicable to non-specific protein and fever therapy We do not recommend their use

Diet.—The diet should be well balanced and should contain sufficient calories to restore the body-weight to normal in patients underweight, while for obese patients it should be designed to ensure the necessary reduction in weight Small frequent meals attractively served will help to stimulate appetite. There are no contra-indications to any particular article of diet and there is no sound reason for believing either that nutritional deficiency is the cause of rheumatoid arthritis or that any food factor has any specific curative value. The need for an adequate intake of protein and an ample supply of vitamins and minerals is based on the general physiological principles which govern the dietetic requirement of a patient suffering from a chronic wasting disease in which metabolism may be further increased by fever A liberal fat allowance should be prescribed in the shape of milk (up to 2 pints daily), cream, eggs and bacon. By this means the required intake of first-class protein, phosphorus and calcium will also be assured. An average helping of meat or chicken at one meal and a fish or egg dish at another should be allowed Ample fresh fruit and vegetables are indicated. In the acute stage when digestion and appetite [illegible] impaired these should be served in the form of [illegible] amount of starchy food such [illegible] is usual to [illegible] if this is ne[illegible]

Gastro[illegible] toxic produ[illegible] the bowel might be a factor in the ætiology of rheumatoid arthritis There is no satisfactory evidence in support [illegible] forms of treatment, such as colonic lava[illegible] no longer be recommended. Constipatic[illegible] administration of small doses of liquid p[illegible] day, supplemented if necessary by a mild laxative such as senna or cascara Unnecessary purgation should be avoided.

Endocrine Glands.—In only a small proportion of cases of rheumatoid arthritis can clinical evidence be found favouring the presence of some abnormal function in one or other of the endocrine glands. The dramatic therapeutic effects of corticotrophin and cortisone do not necessarily indicate that disease of the pituitary gland or the adrenal gland is present in rheumatoid arthritis. Thyroid extract and œstrogenic preparations should be prescribed in cases

of arthritis only if the appropriate symptoms of glandular deficiency are present.

Local Treatment.—During the acute stage of rheumatoid arthritis the affected joints are swollen and exquisitely tender. The slightest movement is accompanied by severe pain and the muscles moving the joints are continuously in spasm. The patient soon discovers the position of greatest ease for the throbbing joints, and is often aided by sympathetic relatives, who little realize that by placing the joints in the flexed positions of the patient's choice they are preparing the way for the establishment of the deformities which are only too commonly the permanent legacy of rheumatoid arthritis. Such a patient lies with flexed knees, flexed hips, flexed elbows. The forearms and hands are laid on the chest, the wrists in a position of palmar flexion, and the feet are allowed to remain plantar flexed for lengthy periods. As the disease progresses, peri-articular and intra-articular adhesions form and movement becomes progressively more limited.

There are two fundamental principles underlying local treatment during the active stage of the disease. The first is the prevention of deformity and the second is the maintenance of function. The spasm of the surrounding muscles is Nature's attempt to immobilize the inflamed joints. As a result of the long-maintained position of flexion, the flexor groups of muscles undergo compensatory shortening and thus still further limit the range of movements. Pain, therefore, must be relieved. It has already been emphasized that analgesics in adequate dosage are essential, but this alone will not suffice The affected joints must be completely immobilized in order to avoid stretching of the inflamed structures, and this is most satisfactorily obtained by application of properly fitting splints. The relief obtained by fixation in such splints is of great therapeutic value, as it allows the patient to sleep without the large doses of sedatives previously required, with consequent improvement in the mental outlook. The muscles, relieved of their burden by the splint, relax. Thus, the fundamental principle of rest must be applied locally to each affected joint if the patient is to enjoy the mental and physical relaxation so essential to his well-being.

Light, easily removable, perfectly fitting splints can be made quickly and simply with muslin bandages impregnated with plaster of Paris. The technical details for their manufacture are given in the Appendix. Whenever possible, the splints should be skin-tight, to ensure complete immobilization of the joints, since the slightest movement within the splint will lead to the return of pain and spasm In very thin patients it may be necessary to pad the bony prominences. This is best done by means of small pieces of chiropodist's felt, which are easily cut to shape and adhere to the skin. Before applying the plaster the skin should be oiled or the limb encased in stockinet, which forms an effective lining to the splint. Since in some of the more severe cases ankylosis may take place in spite of treatment, the splint should hold the joint in the position which will produce the best functional result, should this occur. For example, the wrist should be put up in slight dorsiflexion, the foot midway between dorsi- and plantar-flexion.

Although we believe that splints made by the plaster technique are ideal, their application requires some degree of technical skill, and other materials may be found more convenient Aluminium can readily be cut and shaped to form a splint for any joint, and can be purchased in sheets of the correct

thickness for this purpose. Plastic materials, malleable on heating, are now available which can be used for the manufacture of light waterproof splints. Further experience in their handling is required, but they may well prove to be of considerable value when splints of a more durable character are necessary.

The use of properly fitting splints is a most important advance in the treatment of the joints in rheumatoid arthritis. By this means swelling is reduced more quickly and pain relieved more effectively than by any other method. Some authorities believe that the danger of fibrous ankylosis is most likely to be avoided if splints are removed daily and gentle active movements are encouraged. Others feel that this danger has been exaggerated and that in the acute stage symptoms will subside more rapidly if complete immobilization is maintained for one to two weeks. After this initial period splints are removed once or twice daily for active exercises (see Appendix). Whichever method is adopted, the patient should be taught to contract his muscle with the splints in position (static contractions). Active exercises should be preceded by heat because of its value in easing pain and relaxing muscle spasm. Portable radiant heat cages or lamps can be used for this purpose. Moist heat in the form of simple hot fomentations or kaolin poultices is also valuable as a preliminary to exercises. Light stroking massage may also be used with benefit at this stage. When skilfully applied to the muscles controlling affected joints, spasm may be reduced or abolished. The combination of heat and light massage may be more effective than either form of treatment given alone. When the joints of the lower limbs are involved, a resumption of walking must be delayed until muscular control has been restored by the systematic use of carefully graded exercises. The more strenuous forms of physical treatment should not be given until the activity of the disease has diminished. They are discussed in the next section.

Hydrocortisone acetate in suspension can be injected intra-articularly and has proved a useful means of controlling inflammation locally. Following injection, pain is reduced and effusions may subside. The duration of relief varies from a few days to two or three weeks. Repeated injections are well tolerated. This treatment is particularly useful when progress is retarded by persistent pain and swelling in one or two joints, particularly the knees. Effusions, if present, should be aspirated before the injection is given. Strict asepsis must be observed, as invasion of the joint by bacteria may be facilitated in the presence of hydrocortisone. For the treatment of large joints, such as the knee, 25 to 50 mg. should be given; 2 to 5 mg. may prove adequate for the small peripheral joints in the hands and feet. The interval between injections will vary according to the duration of relief obtained. It has been claimed that, in patients receiving cortisone by mouth, local treatment of one or two persistently painful joints may enable the daily dose to be reduced.

There is no doubt that the intra-articular injection of hydrocortisone is of value in the local treatment of the joints in rheumatoid arthritis.

SUBACUTE STAGE OF RHEUMATOID ARTHRITIS

The patient may reach the subacute stage after weeks or months of treatment in the acute stage. Alternatively the disease may commence insidiously and the patient presents himself for treatment in the subacute stage. Characteristically one or more of the joints is swollen and painful, a considerable degree of asthenia and muscular wasting is generally present, fever is absent, but the sedimentation rate is raised to a figure of 30 to 50 mm. in one hour. In such cases the investiga-

joints under water is particularly beneficial. Re-educational exercises, under the guidance of a properly trained physiotherapist and devised according to the individual patient' [illegible] tion of deformity [illegible]

Physiotherap [illegible] therapy can be used by the patient at home. These methods can be taught during the patient's stay in hospital or on attendance as an out-patient. Simple [illegible] Heat [illegible] ibed in [illegible] ince of following a regular régime of rest and exercise must be strongly emphasized Local rest is attained by splints worn at night and, if necessary, for periods during the day. Patients should lie down for an hour in the middle of the day, [illegible]

fully immersed at a temperature between 98° and 105° F. This should be followed by an hour's rest wrapped in towels. Immersion baths of this type should not be used more than three times a week in the case of debilitated patients. In the case of housewives, rearrangement of kitchen and household equipment and the provision of a number of suitable aids can do much to take the load off damaged joints. The regimen of physiotherapy in the home should be adjusted and controlled by regular review of the patient's progress.

CHRONIC STAGE OF RHEUMATOID ARTHRITIS

If all cases of rheumatoid arthritis were correctly treated in the acute and subacute stages, deformities would be met with much less frequently. However, much can now be done to improve the lot of those patients in whom the active phase of the disease has passed but in whom marked deformities have arisen in the joints.

In addition to the physiotherapeutic methods already described, special procedures are required for the correction of deformities and restoration of function, which are wholly orthopædic in nature and may include surgical intervention in a small proportion of cases (see Surgery in Arthritis, p. 767).

Treatment of Deformities.—The commonest deformities are fixed flexion of the hips, knees and elbows, limitation of abduction and rotation in the shoulders, limitation of movement or ankylosis of the wrists in palmar flexion and of the ankles in plantar flexion, subluxation of the metacarpo-phalangeal joints with ulnar deviation of the fingers, subluxation of the interphalangeal joints, flat foot and hallux valgus. The joints usually become fixed in the position which is most comfortable to the patient during the acute stage, as has been previously mentioned. The maintenance of the joints in these positions for long periods leads to the formation of intra- and extra-articular adhesions, destruction of the cartilage becomes complete, and in the more progressive cases bony ankylosis ensues

A brief description of some of the methods used for the treatment of the more common deformities will be given, but for full information on this subject the reader is referred to the works of those orthopædic surgeons who have made a special study of the chronic rheumatic diseases

Weight Extension —This method is used in overcoming flexion deformities

of the knees and hips. The limb is placed in a modified Thomas' splint and about 10 to 15 lb. extension applied in the usual way If a Balkan beam is available, the limb in the splint is slung from this This method does nothing to allay muscular spasm and the patient may experience considerable pain.

Serial Plasters.—One of the most important advances in the technique of correction of deformities is the use of serial plasters (see Appendix). It is of particular value for the correction of flexion deformities of the knees, but can be used in any joint which is accessible to the application of plaster In the case of the knees, a complete plaster is applied to the limb and bi-valved when dry to allow of movement of the joint and massage to the muscles After three to six days' complete rest in the plaster, it is found that the knee is now capable of an extra few degrees of extension. This gain is consolidated by the application of a new plaster. After four to six plasters have been applied, complete extension will frequently have been attained In more resistant cases manipulation under a general anæsthetic may be required before a full range of movement can be restored to the joint. The advantages of serial plasters are that no strain is thrown on the articular structures, the muscles are put at rest, spasm is overcome and pain is relieved.

Manipulation.—Manipulation under a general anæsthetic is of value in properly selected cases of rheumatoid arthritis Great care must be exercised if the bones are markedly decalcified, otherwise a fracture may result Certain joints react well to manipulation—knees, hips and shoulders Results are less certain in the wrists and ankles, and good seldom comes of manipulation of the elbows. The presence of severe cartilaginous damage may not preclude some return of movement, but the after-treatment must be prolonged and weight-bearing avoided for some weeks

Peri-articular Infiltration and Intra-articular Injection.—When minor degrees of pain and disability are present, local infiltration of the peri-articular structures, on one or more occasions, with ½ per cent solution of procaine according to the technique described for the treatment of fibrositis (see p 763), followed by heat and movements, may be sufficient to banish pain and restore full function.

The intra-articular injection of hydrocortisone (p 745) has proved as useful in the more chronic phases of the disease as it has in the acute stage, so long as symptoms are due to persistent inflammation rather than to structural changes in the joint structures The technique employed is similar to that already described.

Splints and Crutches.—In cases where abduction has become limited in the shoulder but where the degree of activity precludes manipulation under an anæsthetic, full movement may be restored by the use of an aeroplane splint. When first applied, it is adjusted so as to hold the arm in the position of maximum abduction compatible with comfort The arm is bandaged firmly to the splint, which must be well padded The rest obtained will relax spasm and in a few days more abduction becomes possible The splint is now adjusted to hold the arm in the new position This process is continued until full abduction has been restored. The underlying principle is exactly similar to that of the serial plaster method Heat and movement to the joint and massage and exercise for the muscles are employed daily

In more severe cases the damage to certain joints may be of such a degree that appliances are necessary to supplement the impaired function before the patient can regain the power to walk The simplest of these is crutches, which

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arthritis are valueless in osteoarthritis Similarly vaccines, non-specific protein shock therapy, cortisone and corticotrophin play no part in its treatment.

Local Treatment.—Physiotherapy and not drug therapy is the essential feature of the treatment of osteoarthritis By this means, muscular spasm can best be relaxed and pain relieved. Physiotherapy enables movements of the joints to be undertaken more freely with concomitant improvement of function [illegible]

in about 50 to 60 per cent. of cases in a carefully controlled series. In view of possible dangers of radiotherapy, this method should only be used when all other forms of treatment have failed to give relief and where pain is severe and persistent.

Massage should be given to the muscles surrounding the joint with a view to improving the local circulation and relieving pain and muscular spasm Massage should not be applied to the joints themselves as it has no beneficial [illegible] may even prove harmful. Where wasting of muscle is present, active [illegible]

which relaxes spasm and eliminates the effect of gravity, thus enabling movements to be carried out with the minimum of pain. The undercurrent douche should be applied at the same time.

For those unable to visit a spa, a hot bath and the other measures described in the section on Physiotherapy at Home (p. 748) are useful substitutes in enabling the patient to obtain the benefits of heat and movements.

Peri-articular and Intra-articular Injections.—*Good* results have been claimed to follow the injection of a variety of substances into the joint cavities in osteoarthritis Controlled clinical trials have shown that, if improvement follows such treatment, it bears no constant relationship to the material injected.

Intra-articular injection of a 1 per cent. solution of procaine combined with infiltration of tender areas in the peri-articular soft tissues is a useful method of treatment worthy of trial in cases of osteoarthritis in accessible joints The amount required will vary from 2 to 3 ml in smaller joints to 15 to 20 ml in the case of the hip or shoulder. If relief of reasonable duration is achieved, the [illegible] should be [illegible]

the cavities of joints are described on p. 879.

Orthopædic Procedures.—Manipulation under a general anæsthetic may be a valuable procedure, but it must be employed with great caution and only in selected cases where there is considerable pain and limitation of movement with only moderate bony changes. In such a case, peri-articular adhesions and capsular thickening are believed to be largely responsible for the disability which is present and much benefit may be obtained from manipulating the joint in a gentle manner under full surgical anæsthesia This must be followed by daily movement of the joint preceded by heat

Mechanical appliances for the relief of weight-bearing joints may be necessary if the measures already outlined fail to give relief The types most frequently used are caliper splints constructed to take the weight off the knee or hip or a steel brace to support the spine These appliances are expensive and should only be ordered on the advice of a competent orthopædic specialist and should be fitted by a trained technician The indications for surgical treatment are discussed on p. 767.

CHRONIC MENOPAUSAL ARTHRITIS

(Chronic Villous Arthritis, Climacteric Arthritis)

There is a form of arthritis which occurs commonly in women about the time of the menopause. Those affected have, as a rule, been considerably overweight for some years and show signs of the subthyroid state The joints principally affected are the knees, but minor changes are usually present in the hands In the early stages of the disease the affected joints are swollen and painful owing to thickening of the peri-articular structures, hypertrophy of the synovial membrane or less commonly to the presence of fluid in the joint cavity The condition is a proliferative synovitis rather than an arthritis, since radiological examination reveals little or no bony change. In untreated cases the disease slowly progresses until typical signs of osteoarthritis occur

Various factors appear to play a part in the ætiology of this disease, but the most important from the point of view of treatment is obesity. Menopausal endocrine deficiencies may influence the onset directly by giving rise to premature senility and the early appearance of degenerative changes in the joints, or indirectly by leading to obesity

The condition is one which is peculiarly amenable to treatment in the early stages. The first step must be to reduce the strain thrown upon the knees by excessive weight. If this object is attained by careful regulation of the diet, and where necessary, by the administration of thyroid, combined with suitable general and local treatment, the appearance of the cartilaginous and bony changes of osteoarthritis may be delayed A suitable diet of low caloric value is prescribed, and the patient must be impressed with the importance of adhering to it strictly For details of a suitable diet see p 325 A small dose of thyroid, such as 30 to 60 mg (½ to 1 gr) twice a day, should be administered should the patient show any evidence of hypothyroidism Otherwise it is valueless The dose must be adjusted to suit the requirements of each individual case Drugs have little beneficial effect in chronic menopausal arthritis with the exception of the analgesics The peripheral circulation is often sluggish and the skin is tacked down to the subcutaneous tissues Tender areas are commonly present around the joints and in the scapular region The injection of procaine and the application of heat followed by massage, as already

described on p. 749, do much to improve the circulation, disperse the fibrositic

reduction in weight has been secured. Crêpe bandages or Elastoplast should be applied to the knee in order to maintain an even pressure, which will aid the reabsorption of effusion and provide support during weight-bearing. These should be retained when the patient returns to active life and until the quadriceps muscles have regained their normal tone. Static muscular contractions should be practised during the time when the patient's activities are restricted. Spa treatment is particularly suitable for patients with menopausal arthritis as the physiotherapeutic and hydrological facilities available are of the utmost value. When very marked synovial proliferation is present, resulting in nipping of fringes between the articular surfaces, surgical intervention may become necessary (see p 767).

When the disease is treated early, the prognosis is good. If osteoarthritic changes are established when the patient is first seen, the treatment is the same as already described for that disease on p. 751.

SPONDYLITIS

Arthritis affecting the spine occurs in two main forms—spondylitis osteoarthritica (spondylosis deformans) and ankylosing spondylitis (spondylose

radiological examination, are now considered to arise as a result
degeneration of the intervertebral disc,
between the vertebral bodies. The
posterior spinal articulations may also
which alters the anatomical relationships of the articular facets. Both conditions are commonest in those whose occupation throws a heavy strain on the spine, e g. miners working at the coal face. Injury, heavy lifting, obesity and deterioration in posture may all play a part in the causation of spondylitis osteoarthritica Radiological changes are frequently present before symptoms appear. Pain may arise from abnormal stresses and strains falling on the spinal ligaments and posterior articulations. It may also arise from pressure on nerve roots caused by narrowing of the vertebral foraminæ or protrusion of the intervertebral disc. It is probable that many cases of brachial neuralgia and sciatica (p 831) and a proportion of cases of acute lumbago are caused by lesions of the intervertebral discs

In the majority of cases of backache due to the changes described, pain is intermittent in character, but attacks tend to increase in frequency as age advances.

Treatment.—In milder cases, the application of hot packs over the affected area will give relief. Massage should not be prescribed until the more acute symptoms have subsided, when it may be used with benefit. At this stage the various forms of baths already described are valuable. In more severe cases,

where pressure on the nerve roots is causing pain, the patient should be put to bed and the spine kept flat by the insertion of fracture boards under the mattress. Where arthritis of the cervical spine is giving rise to brachial neuralgia, relief may be obtained by applying weight extension. The weights are attached to a cord running from a head sling through a pulley at the top of the bed. Ten to fifteen pounds weight is usually sufficient Complete immobilization of the cervical spine in a plaster cast for several weeks may be the only form of treatment which gives relief in more intractable cases The fitting of a spinal support may be of value in the more chronic cases Local heat should be used in one or other of the forms already described.

In cases of osteoarthritis of the spine which fail to respond to these measures, it may be necessary for the patient to change to a less strenuous form of employment.

Ankylosing Spondylitis.—This is a disease mainly of early adult life and is much more common in males Its incidence is relatively small, but when it arises it is an extremely serious condition which may completely incapacitate the sufferer and even endanger life The pathology is so similar to that of rheumatoid arthritis in the peripheral joints that it has been called rheumatoid arthritis of the spine, although in the opinion of a number of observers it is an entirely different disease. The onset of symptoms referable to the spine is preceded by a period during which the patient complains of vague pain in his muscles and joints. The estimation of the sedimentation rate at this time may suggest the presence of some infective process, and radiological examination of the spine and pelvis may show the early changes of ankylosing spondylitis The disease affects particularly males in the early twenties, well developed and of an active mode of life. In the majority of cases the first joints to show radiological changes are the sacro-iliacs, which become ankylosed very early in the course of the disease. As the disease progresses the intervertebral and costovertebral joints are involved, the spine becomes rigid and the thoracic cage immobile a few severe cases the disease may spread to involve the hips and shoulder more rarely the elbows, hands, knees and feet The joint changes are accompanied by generalized muscular wasting In the early stages patients are usually mbulatory, with the result that, owing to decalcification and softening of the ertebral bodies, the spine assumes a kyphotic position, and unless treatment is nstituted early this deformity will become permanent owing to the deposition of calcium in the ligaments and capsules of the joints The calcification and later ossification of the joint capsules is a characteristic feature

General Treatment—Although the cause of the disease is unknown, a scheme of treatment similar to that described in the section on rheumatoid arthritis must be adopted (see p. 733), including application of all the measures already detailed to raise the general resistance and improve the health of the patient In active cases, with marked systemic symptoms, an initial period of rest in bed may be required, but movements of the spine and thoracic cage must be maintained by daily active exercises Prolonged periods of recumbency should be avoided, as experience shows that movement is better preserved in these patients when they are ambulant

Drugs should be used with discretion, as in rheumatoid arthritis, analgesics again being the most valuable Similar considerations to those discussed in connection with rheumatoid arthritis on p 735 govern the use of phenylbutazone, gold, cortisone and corticotrophin

Local Tre... are very satisfactory. ... whatever the stage of tl ... leformity, pain may be markedly relieved. The best results follow a course of daily treatment lasting two weeks Treatment is applied to the whole spine and sacro-iliac joints. Even in very early cases it should never be confined to the lumbar spine and sacro-iliac regions. The skin dose on all fields is 1,500 r. The course should not be repeated except in special circumstances, but should the hips or shoulders become painful at a later date, further radiation may be applied to these joints In young women, the sacro-iliac regions should be avoided in view of the danger of causing sterility.

In early cases with no deformity the disease process may be completely arrested and full movement may be regained. The maintenance of good posture must be ensured. When radiological changes are confined to the sacro-iliac joints, no period of rest in bed may be necessary, but postural and breathing exercises must be performed daily. If, at the end of one year, there has been no recurrence of symptoms, routine exercises may be discontinued. In more advanced cases, where radiological examination shows no ossification of the spinal ligaments, but where posture is already poor, a period of two to three weeks' rest in bed combined with postural exercises is necessary. Fracture boards should be placed under the mattress. On getting up, these patients should be fitted with a spinal brace, which should be worn until muscular power has been completely restored. The brace is removed several times daily and active exercises performed In advanced cases with established deformity, the relief of pain and stiffness following radiotherapy greatly facilitates the restoration of good alignment by the use of serial plaster shells In cases with a marked kyphotic deformity which cannot be corrected otherwise, spinal osteotomy may be used to improve postural alignment. These patients may have to wear some form of orthopædic support permanently. Recognition of the disease at an early stage, followed by adequate treatment, will effectively ...

... to be completely arrested, ... re the maintenance of good posture.

STILL'S DISEASE

A rheumatoid type of arthritis occurs occasionally in children below the age of ten. It is accompanied by fever, leucocytosis, glandular enlargement and splenomegaly There is a tendency for the infantile proportions of the limbs to ... the disease processes. The ... ular ... irse.

Although dramatic remissions have been recorded occasionally, the results of treatment are generally held to be less satisfactory than those obtained in ordinary rheumatoid arthritis. Corticotrophin and cortisone are effective in suppressing the symptoms of Still's disease, but their use in treatment is limited by the same considerations already discussed in relationship to rheumatoid arthritis (p. 739).

Diseases of Connective Tissue.—In the group of conditions defined by Klemperer and his colleagues in 1942 as diseases of collagen, a widespread lesion of connective tissue is the common factor linking disorders with diverse clinical features and very different prognoses. The lesion affects all components of extracellular connective tissue and for this reason diseases of connective tissue is a more accurate description than collagen diseases, which suggest a specific lesion of collagen alone. The histological appearance of what is best described as fibrinoid change rather than fibrinoid degeneration of connective tissue arises from the disintegration of collagen fibres accompanied by the deposition of pink staining material, rich in polysaccharides. Fibrinoid change is invariably accompanied by signs of an inflammatory reaction in the surrounding tissues. The diseases in which the lesion is always present are rheumatic fever, rheumatoid arthritis, polyarteritis nodosa, disseminated lupus erythematosus, scleroderma, dermatomyositis and serum sickness. The ætiology of these conditions is unknown, but all show evidence of systemic disturbances as well as the local lesions upon which the diagnosis is based. Symptoms referable to the joints may be present at some time in all members of the group, and with the exception of rheumatic fever and serum sickness, the course of the disease tends to be prolonged. Rheumatic fever, serum sickness and rheumatoid arthritis have been dealt with elsewhere. The other members of the group are relatively uncommon, but are important to the physician interested in rheumatic diseases since they present a difficult diagnostic problem when joint symptoms are also present.

Polyarteritis Nodosa and Disseminated Lupus Erythematosus.—Until the advent of the pituitary and adrenal hormones, treatment for these two conditions was entirely symptomatic. No available drug had been shown to alter the course of either, and the outcome was invariably fatal. A dramatic response to corticotrophin, cortisone and hydrocortisone regularly occurs, and in severe fulminating cases their administration may be life saving. Acute manifestations can be suppressed, and patients restored to a useful functional level. It is now clear, however, that these hormones are in no way curative. Continuous maintenance therapy is essential. The presence of impaired renal function, common in both diseases, before treatment is of serious significance as these patients frequently deteriorate while receiving the hormones. The drug most commonly used has been cortisone. Large initial doses are often required to control acute symptoms. The drug is given by mouth and 300 to 400 mg. daily may be necessary. The dose is gradually reduced until a satisfactory maintenance dose is reached. This is not infrequently in the region of 100 to 150 mg. daily. Moderate or marked signs of hyperadrenalism will occur in many of these patients, but this disadvantage must be accepted if control is to be maintained. This is justifiable in diseases which frequently have a fatal outcome. It is not yet certain that life can be prolonged by hormone therapy, but the great increase in comfort which accompanies their administration fully justifies their continued use.

Scleroderma and Dermatomyositis.—The results of hormone therapy in these two diseases have been disappointing. In scleroderma little alteration in the skin condition has been observed. This disease does not as a rule cause marked systemic upset and the use of high doses of cortisone or corticotrophin is not justified by the results obtained. In dermatomyositis, acute exacerbations

with marked weakness of the muscles, not infrequently involving the respiratory muscles, may endanger life. In these circumstances the use of cortisone or corticotrophin may tide the patient over the crisis. Adequate doses must be used initially. Slow reduction with a view to withdrawal should be started when acute symptoms have been controlled

GOUT

Gout is a disease characterized by recurrent attacks of acute pain and swelling,

metabolism responsible for the increased production of uric acid. Recent studies suggest that the prolonged use of uricosuric agents, by ridding the body of excess uric acid, may substantially reduce the number of attacks. The disease is familial in the majority of cases. Raised levels of plasma uric acid in relatives who have never suffered from gouty arthritis suggests that factors other than the abnormality of purine metabolism are concerned in the production of clinical gout. The almost complete immunity of women before the menopause suggests that the sex hormones may play some part.

The metatarso-phalangeal joint of the big toe is the site of the first attack in 80 to 90 per cent. of cases. Attacks may be separated by long intervals in the early stages of the disease, but increase in frequency as age advances. They are often precipitated by dietetic indiscretion, over-exertion, injury, exposure to cold or a surgical operation. As the disease progresses, uric acid in the form of mono-sodium biurate is deposited in the cartilage of joints and ears, subcutaneous tissues and bursæ. More serious is the deposition of urates in the renal tissues leading to progressive renal failure The plasma uric acid is raised above the upper limit of normal (6 mg per cent. in males and 5 mg. per cent. in females), but the level bears no constant relationship to the frequency or severity of acute attacks. Attacks may be preceded by symptoms of dyspepsia or mental depression and irritability.

Prevention.—With modern methods of management much can be done to reduce the number of acute attacks, shorten their duration and prevent the later complications of the disease such as the development of osteoarthritic changes in affected joints and progressive renal failure. It is doubtful if the imposition of dietetic restrictions is justifiable in males with a family history of gout unless the blood uric acid is shown to be above normal on more than one occasion, but these men should be advised to avoid obesity by exercising moderation in eating and drinking, avoid excessive fatigue and violent exercise, and lead a regular life in the reasonable expectation that the onset of clinical gout may be delayed or avoided.

Treatment.—*Acute Stage.*—During the acute attack of gouty arthritis, pain in the affected joints may be excruciating Some degree of systemic upset

two hours until pain is relieved or diarrhœa starts. In the great majority of cases relief will be obtained within twenty-four to forty-eight hours, especially if treatment is started early in an attack. The total amount of colchicine required varies from case to case, but in general lies between 4 and 8 mg. Patients learn with experience the amount of the drug required to obtain relief without causing unnecessary gastro-intestinal upset. If diarrhœa becomes troublesome before symptoms are relieved, camphorated tincture of opium should be given in doses of 4 ml. (60 min.) after each loose motion. Copious fluids should be drunk (4 to 5 pints) and the diet should consist of eggs, fruit, milk and cereals (see below). Prompt treatment along the lines described will give rapid relief in the majority of cases. When acute attacks are frequent, the regular ingestion of small doses of colchicine, 0·5 to 2 mg. daily, appears to reduce the incidence of acute episodes. Drug tolerance does not develop.

Patients who have experienced a number of acute attacks will come to recognize the premonitory symptoms, and can be instructed to start treatment at once. Rest in bed combined with colchicine in the doses given above may completely abort the attack at this stage.

Colchicine should be tried first in every case, but a small number of patients may prove resistant to this drug. Phenylbutazone has proved effective in a number of such cases. An initial dose of 0·4 g. (6 gr.) by mouth is followed by 0·1 g. (1½ gr.) every four hours until all signs of inflammation in the joint have subsided. Pain is relieved in eight to twelve hours and the drug can be discontinued in three to four days. No significant toxic reactions have been recorded during this short period. The drug causes a marked increase in excretion of uric acid when given over a longer period (p. 736), but its value in the acute attack does not depend on this action but on its analgesic and anti-inflammatory effects. In cases where colchicine is not well tolerated by mouth and phenylbutazone has proved ineffective, colchicine can be given by the intravenous route. The initial dose should be 0·25 to 1 mg. dissolved in 5 ml. sterile normal saline, to be repeated in eight to twelve hours if symptoms persist.

It has been shown that both cortisone and corticotrophin can be used to control acute gout. Corticotrophin is the more effective, but must be given in conjunction with colchicine if relapse on withdrawal of the hormone is to be avoided. This method of treatment is not recommended for routine use, as only exceptional cases will fail to respond either to colchicine or phenylbutazone in the doses specified.

Treatment between Attacks.—Investigations of the metabolism of uric acid in normal persons and sufferers from gout using isotopically labelled uric acid have shown that there is a large increase in the total quantity of freely exchangeable uric acid in the body fluid of gouty subjects. This is due largely to an increase in the production of uric acid from nitrogenous precursors in the diet, including carbohydrates, proteins and fats. Treatment between attacks is based upon partial control of uric acid production by dietary measures and the increased excretion of uric acid by the kidneys induced by the administration of uricosuric drugs. The degree and duration of dietary restriction, the amount of the chosen drug to be given and the period over which it should be administered will vary from case to case and can only be determined by a careful consideration of all the circumstances in each individual patient.

Diet.—In view of the formation of uric acid from many components of the diet, there is no justification for severe restriction of purines and protein. In

general, the diet should be low in purines and fat and should not exceed the caloric needs of the patient. Foods with a high purine content should be forbidden. The following contain large amounts of purines: sweetbreads, liver, kidney, brain, heart, anchovies, sardines, meat extracts, herring roe, whitebait, sprats, smelts. Meat, game, poultry and fish, with the exceptions noted above, contain only moderate amounts of purine and can be used in reason. Peas, beans, lentils and spinach also contain moderate amounts of purine, but other vegetables and fruits contain little and can be taken freely, with the exception of spinach, rhubarb and strawberries. These contain oxalates which it is thought may facilitate the precipitation of urates. Milk, cheese, eggs, cereals, bread, sweets, chocolates, jellies, cocoa, coffee and tea do not contain purines which lead to uric acid formation Their use will be limited only so far as it is necessary to restrict the caloric value of the diet. Fatty foods, cream, butter and margarine should be restricted, both because of their caloric value and because of the evidence that fat influences adversely the excretion of uric acid. The treatment and prevention of obesity is of prime importance. Occasionally patients find that certain articles of food or drink have a specific effect in precipitating an acute attack, and these must obviously be omitted from their diet. Alcohol is best avoided, but total prohibition is not always justified as teetotallers can develop classic gout and most alcoholics never suffer from the disease.

Drugs.—A number of drugs increase the excretion of uric acid by the kidneys. These include cinchophen, acetyl-salicylic acid, sodium salicylate, phenylbutazone, corticotrophin, cortisone and probenecid (Benemid, P-(di-n-sulfanyl)-benzoic acid) Cinchophen is no longer recommended on account of its potential dangers. The dangers of long-term administration of phenylbutazone have already been discussed (p 736). Corticotrophin and cortisone are not used as uricosuric agents because of undesirable hormonal effects. The drugs of [illegible] long

times

acid

excretion by 30 to 50 per cent. in g[illegible]

blood uric acid may return to norr[illegible]

clearance of excess uric acid from

diminishing the incidence of renal damage, the most serious complication in chronic gout. Ample fluids should be drunk to prevent deposition of urates in the kidneys, and since precipitation occurs most readily in acid urine, ample alkalis should be prescribed. Neither drug invariably prevents acute attacks, but there is now considerable evidence to show that they will greatly diminish their number and may eventually lead to prolonged periods of freedom Occasional toxic reactions from probenecid have been reported, in the form of gastro-intestinal symptoms and skin rashes. The recognized toxic effects of sodium salicylate occur in a proportion of gouty patients on maintenance therapy. Since salicylate therapy is much cheaper than treatment with pro[illegible] should be tried first

will be

to a spa

y in the

majority of patients

If a surgical operation becomes necessary in a gouty patient, colchicine in

doses of 0 5 mg. ($\frac{1}{120}$ gr.) thrice daily should be given for three days before operation *and for three days after, in the hope that an acute attack following the* operation may be prevented

Where tophi have become large and unsightly, or have ulcerated through the skin, they can be removed surgically with satisfactory results.

[illegible] the outlook for [illegible] ease in the form [illegible] be prevented or at least delayed.

NON-ARTICULAR RHEUMATISM

("*Fibrositis*"—*Muscular Rheumatism*—*Myalgia*)

Introduction.—No satisfactory classification has ever been devised of the various disorders which give rise to pain and stiffness, but which are not associated with obvious changes in the joints. This is due to lack of knowledge both of the ætiological agents responsible and of the pathological changes to which they may give rise The term "fibrositis" was first used by Sir William Gowers in 1904 to denote the hypothetical inflammatory changes in the fibrous structures of the lumbar muscles during an attack of lumbago. In 1920, Stockman described the histological appearances in biopsy material obtained from various affected sites and on that basis defined "fibrositis" as a "condition of chronic inflammation of the white fibrous tissue of fascial aponeurosis, sheaths of muscles, and nerves, ligaments, tendons, periosteum and subcutaneous tissues, occurring in all parts of the body and giving rise to pain, aching stiffness and other symptoms, the result of preceding general infections, or local inflammations or injuries". A number of experienced investigators have failed to confirm his histological findings In contrast, the signs of inflammation in connective tissue can invariably be demonstrated in the so-called collagen diseases or diseases of connective tissue, e g. rheumatic fever, rheumatoid arthritis and ankylosing spondylitis

In the present state of our knowledge it may be best to abandon the term "fibrositis" with its implication of an inflammatory basis, in favour of a more non-committal term such as "non-articular rheumatism" for the miscellaneous group of conditions which may give rise to pain and stiffness without demonstrable changes in the joints *A number of authorities now hold the view that* many painful conditions included in this group are in fact due to primary changes in joints or their immediately related structures, although radiological examination may fail to reveal any deviation from normal This change in outlook is well illustrated in the case of painful conditions arising in relation to the spine, formerly believed to be due to "fibrositis" (lumbago, sciatica, cervical fibrositis, brachial neuritis, etc.) The opinion is now widely held that the [illegible] po [illegible] th [illegible] found or derangement of joints or related structures demonstrated by radiological examination. It is in connection with this group that certain ætiological factors will be discussed

Ætiology.—Although the ætiology of non-articular rheumatism is still unsettled, common experience has shown that certain factors are of particular

significance. More than one may be concerned in the individual case, and until all are adequately dealt with treatment may produce only temporary alleviation of symptoms, to be followed by relapse on resumption of an unsuitable occupation or return to an uncongenial environment.

Cold.—Exposure to cold and damp are universally recognized as factors which commonly precipitate an acute attack, especially in those people with a predisposition to the disease This is particularly the case if the patient becomes chilled after physical effort or is exposed to a draught which causes a sudden drop in the local skin temperature.

Physical Fatigue.—Fatigued muscles are peculiarly prone to become the seat of an attack Chronic fatigue brought on by continued over-use of specific muscle groups is more important in this respect than general fatigue following excessive physical exertion. This probably explains the widespread occurrence of non-articular rheumatism in certain occupations where long-continued repetition of certain movements is common.

Trauma—The effects of trauma and fatigue cannot be clearly separated. [illegible]

Posture.—Poor posture is associated with muscular imbalance, which results in chroni[illegible] Such local fatigue is accompanied b[illegible]". Local treatment in such [illegible]on of faulty posture. It should be remembered that postural strains occur both in obese and slender subjects.

Infection—Muscular pain and tenderness are prominent features in the acute phase of many general infections. It has been stated that tender areas in the muscles may persist after such infections and form a basis for future attacks of " fibrositis ". Epidemics of " stiff neck " have been reported in this country among industrial workers. This form of epidemic myalgia is believed to be due to a virus infection

The fashion of incriminating a focus of infection as a cause of non-articular rheumatism is now less popular This possibility must, however, be borne in mind in cases which fail to respond to adequate treatment or where attacks have been repeatedly associated with acute infections.

Metabolic Disorders—In a few cases of non-articular rheumatism there appears to be a gouty basis for the condition, and estimations of the blood uric acid reveals figures persistently above normal. These cases are usually of a chronic nature. A definite association between attacks and the indulgence in certain types of food or drink may give a clue to the diagnosis Attention to diet and the administration of the drugs used in gout (see p. 758) will be an important feature in their treatment.

In the majority of cases of non-articular rheumatism there is no satisfactory evidence of disordered function of the endocrine glands In some cases of hypopituitarism and hypothyroidism painful areas in the subcutaneous tissues occur (panniculitis). The routine administration of endocrine preparations is to be deplored

A few words must be said at this stage about certain conditions where a [illegible]

Psychoneurosis.—Many patients complaining of muscular pain and stiffness have no local organic basis for their symptoms, which are an expression of emotional tension or mental conflict The use of physical methods of treatment [illegible]

Referred Pain.—It has been clearly shown that lesions in deep structures can give rise to pain and spasm in anatomically related muscles and in muscles distant from the lesion but with a nerve supply from the same segment of the cord. These symptoms may mask the presence of the primary lesion and lead to an erroneous diagnosis of non-articular rheumatism. In these cases local treatment of the painful muscles may give sufficient relief to perpetuate the mistake.

Summary.—From what has been said above, the term non-articular rheumatism used in clinical medicine covers a variety of lesions of known and unknown ætiology which give rise to pain, stiffness, aching and limitation of movement.

The diversity of the causes of such symptoms emphasizes the need for a careful history and a complete physical examination in every case The application of a rigid clinical discipline will reveal causes capable of correction in many cases. *In addition it will eliminate cases of functional origin which* would otherwise be labelled "fibrositis" and relegated to the physiotherapy department, a procedure harmful both to the patient and the physician in charge of the case.

Treatment.—Acute Stage.—In the absence of an accurate knowledge of the underlying pathology, treatment of the acute attack of non-articular rheumatism must still be based to some extent upon empirical methods If pain and spasm can be relieved, active movements can be started earlier, and disability may be cut short. General and local measures should be combined to achieve this object. Analgesics should be prescribed in full doses. Aspirin in doses of 1 g. (15 gr) combined with 15 mg ($\frac{1}{4}$ gr.) of codeine four-hourly will suffice in most cases Tension should be removed from the painful structures by arra [illegible]
permits [illegible]
of the r [illegible]
of choi [illegible]
part. [illegible]
household (hot-water bottles, linseed or kaolin poultices, the use of a hot iron [illegible]

points or primary "myalgic lesions" It must be borne in mind that these tender points may lie outside the area in which the patient feels his pain, but pressure on them will reproduce the symptoms of which he complains. These areas should be infiltrated with 2 to 5 ml. of 1 per cent. procaine in normal saline. Accurate location is essential and a final decision on the site of injections [illegible]

be able to resume his ordinary activities almost at once. The treatment should be followed up by a course of heat, massage and exercises. If the best results are to be obtained, treatment should be administered daily for at least a week [illegible]

[illegible] patients who fail to respond to the above measures or who have recurrences of symptoms. The avoidance of chilling is important in every case, and in patients subject to recurrent acute attacks and whose work involves exposure to cold and wet, especially if combined with general or local muscular fatigue, a change of occupation may be advisable. A conservative attitude towards the removal of septic foci is wise. This question is discussed on p. 735. No particular [illegible] always be given

Subacute and Chronic Stage.—A proportion of cases continue to complain of residual symptoms after the acute attack has subsided. Others never experience an acute attack but suffer from continuous or recurrent pain and [illegible] differentiate between patients whose symptoms are functional in origin and those with a genuine organic basis for their disability Disease of deep structures giving rise to referred pain and tenderness must be excluded by a complete physical examination supplemented by radiological or biochemical investigation when indicated. In chronic cases it is possible that some increase in fibrous tissue in and around muscles, tendons and joint capsules is responsible for the persistence of pain and stiffness. Treatment of chronic non-articular rheumatism, to be effective, must be more vigorous and prolonged than in the acute case. Analgesics, heat, massage, local infiltration of painful nodules and exercise are the principal methods of treatment, but results are less dramatic. Accurate localization and infiltration of tender areas is as valuable as in the acute phase, but injections may have to be repeated on several occasions and should be followed immediately by heat, vigorous deep massage and active exercises. Hydrotherapy is of real value in these cases, since it combines heat, massage and active movement (see p 746) The regimen of a spa is particularly suitable for those patients who can afford it, but most of the benefits of spa treatment can be obtained at home by the intelligent application of the methods described and reorganization of the patient's way of life.

Diet.—There is no specific diet for chronic non-articular rheumatism. Obesity must be corrected. In the exceptional case where there is evidence to support a dietetic or metabolic cause, a bland diet of a lacto-vegetarian type as used in gout (see p. 759) should be prescribed.

Drugs—A large number of drugs have been recommended for chronic non-articular rheumatism, the most commonly employed being iodine, arsenic and sulphur. We believe that the beneficial effects claimed for the use of these drugs have been grossly exaggerated. Where a gouty basis exists, colchicine should be given a trial and the other measures put into effect as described on p. 758.

Convalescence.—Rehabilitation following a severe attack of non-articular rheumatism should be thorough. A holiday at a seaside resort may suffice in milder cases, but complete restoration of general fitness is required in those patients returning to heavy work. This may best be carried out in a residential or day-to-day rehabilitation centre where graduated physical training and games can be used to restore the capacity for hard physical exertion. Much subsequent invalidism and loss of working time may thus be avoided.

It is now proposed to discuss briefly the treatment in certain sites where diagnosis may be difficult or where special forms of treatment should be employed.

Occipital and Cervical Regions.—Pain in the occipital and cervical regions is frequently referred from the cervical spine, where osteoarthritic changes and narrowing of the disc spaces are very common (see p 754), but in a proportion of cases examination will reveal the presence of tender points in the region of the occipital ridge. Pressure on these points causes pain, which radiates over the vault of the skull Careful localization and infiltration of these trigger areas, followed by a short course of heat and massage, will usually give complete relief.

Non-articular rheumatism is an occasional cause of painful stiff neck. Local chilling appears to be a peculiarly potent factor in precipitating the attack. The condition is commonly unilateral, causing wry neck, but both sides may be affected simultaneously. Movement is markedly restricted by pain and muscular spasm. Acutely tender areas are most frequent near the occipital attachment of the trapezius, the superior margin of this muscle midway between the acromion and the occiput, and in the clavicular portion of the sternomastoid. Infiltration of these points may give immediate relief Should symptoms persist or attacks occur frequently, manipulation of the cervical spine may be successful, but possible causes of referred pain such as cervical arthritis, caries, or prolapsed intervertebral disc must be carefully excluded by clinical and radiological

vertebræ causing pressure on the roots of the brachial plexus (caries, osteo-arthritis, spondylitis, osteomyelitis). Various conditions causing pressure on the cords of

band, abnorr

tracted scaler

when the shoulder is retracted and abducted) In all these conditions care-*ful examination will reveal evidence of pressure on the roots or cords of the* brachial plexus, and in the latter group compression of the brachial artery in certain positions of the arm Movements in the shoulder joint will be unimpaired.

If acute traumatic conditions are excluded, the common causes of painful shoulder are :

1. Supraspinatus tendinitis.
2. Subacromial bursitis.
3. Adhesive capsulitis.

be able to resume his ordinary activities almost at once. The treatment should be followed up by a course of heat, massage and exercises. If the best results are to be obtained, treatment should be administered daily for at least a week. A thorough inquiry into possible ætiological factors should be made and commonsense advice given as to how their effects can be mitigated. Radiological examination will be required to exclude diseases or disorders of the spine in patients who fail to respond to the above measures or who have recurrences of symptoms The avoidance of chilling is important in every case, and in patients subject to recurrent acute attacks and whose work involves exposure to cold and wet, especially if combined with general or local muscular fatigue, a change of occupation may be advisable A conservative attitude towards the removal of septic foci is wise This question is discussed on p. 735. No particular [illegible]

always be given.

Subacute and Chronic Stage.—A proportion of cases continue to complain of residual symptoms after the acute attack has subsided. Others never *experience an acute attack but suffer from continuous or recurrent pain and* stiffness of a less intense degree. Such people are usually sensitive to impending changes in the weather and suffer most during cold, wet spells. It is amongst this group that diagnosis is particularly difficult Great care must be taken to differentiate between patients whose symptoms are functional in origin and those with a genuine organic basis for their disability Disease of deep structures giving rise to referred pain and tenderness must be excluded by a complete physical examination supplemented by radiological or biochemical investigation when indicated. In chronic cases it is possible that some increase in fibrous tissue in and around muscles, tendons and joint capsules is responsible for the persistence of pain and stiffness. Treatment of chronic non-articular rheumatism, to be effective, must be more vigorous and prolonged than in the acute case Analgesics, heat, massage, local infiltration of painful nodules and exercise are the principal methods of treatment, but results are less dramatic. Accurate localization and infiltration of tender areas is as valuable as in the acute phase, but injections may have to be repeated on several occasions and should be followed immediately by heat, vigorous deep massage and active exercises. Hydrotherapy is of real value in these cases, since it combines heat, massage and active movement (see p 746). The regimen of a spa is particularly suitable for *those patients who can afford it, but most of the benefits of spa treatment can be* obtained at home by the intelligent application of the methods described and reorganization of the patient's way of life.

Diet.—There is no specific diet for chronic non-articular rheumatism. Obesity must be corrected In the exceptional case where there is evidence to support a di [illegible] of a lacto-vegetarian type as *used in gout* [illegible]

Drugs.— [illegible] chronic non-articular rheumatism, the most commonly employed being iodine, arsenic and sulphur. We believe that the beneficial effects claimed for the use of these drugs have been grossly exaggerated. Where a gouty basis exists, colchicine should be given a trial and the other measures put into effect as described on p. 758.

Convalescence.—Rehabilitation following a severe attack of non-articular rheumatism should be thorough. A holiday at a seaside resort may suffice in milder cases, but complete restoration of general fitness is required in those patients returning to heavy work This may best be carried out in a residential

diagnosis may be difficult or where special forms of treatment should be employed.

Occipital and Cervical Regions.—Pain in the occipital and cervical regions is frequently referred from the cervical spine, where osteoarthritic changes and narrowing of the disc spaces are very common (see p. 754), but in a proportion of cases examination will reveal the presence of tender points in

Non-articular rheumatism is an occasional cause of painful stiff neck. Local chilling appears to be a peculiarly potent factor in precipitating the attack. The condition is commonly unilateral, causing wry neck, but both sides may be affected simultaneously Movement is markedly restricted by pain and muscular

of these points may give immediate relief. Should symptoms persist or attacks occur frequently, manipulation of the cervical spine may be successful, but possible causes of referred pain such as cervical arthritis, caries, or prolapsed intervertebral disc must be carefully excluded by clinical and radiological

numerous and the differential diagnosis may be difficult Root pain, radiating to the shoulder and down the arm, may arise from lesions within the spinal canal (tumours, brachial radiculitis, prolapsed disc) or disease of the cervical vertebræ causing pressure on the roots of the brachial plexus (caries, osteoarthritis, spondylitis, osteomyelitis) Various conditions causing pressure on the cords of the brachial plexus must be distinguished (cervical rib or fibrous band, abnormal first rib, prominent anterior border of scalenus medius, contracted scalenus anticus, compression between the first rib and the clavicle when the shoulder is retracted and abducted). In all these conditions care-

paired.

If acute traumatic conditions are excluded, the common causes of painful shoulder are ·

1. Supraspinatus tendinitis.
2. Subacromial bursitis.
3. Adhesive capsulitis.

Supraspinatus tendinitis.—The ætiology of this condition is unknown, but

the arm has been abducted beyond a right angle. Treatment consists of infiltration of the supraspinatus tendon near its insertion followed by heat and active exercises. In early cases this may lead to complete cure. In long-standing cases

will be limited to a greater or lesser degree. Conservative measures should be given a trial. Infiltration of the bursa followed by heat and graduated exercises may lead to cure, but in many cases more radical measures are required. Radiotherapy gives relief in some cases. Good results have been obtained by washing out the bursa with saline. In cases which fail to respond to these measures

following trauma. In the elderly it is a common complication of fractures of the arm, forearm or hand, when active movements of the shoulder have been neglected during immobilization of the injured limb in plaster. Movement is best restored by a series of gentle manipulations under general anæsthesia.

Lumbar Region.—Pain and muscular spasm in the lumbar region may arise from many causes and may also present a difficult diagnostic problem. It is now generally accepted that the majority of cases of *acute lumbago* are due to lesions of the intervertebral discs, even though sciatic pain may be absent.

should be followed by exercises for the extensor muscles of the spine, and the patient should receive instruction in those methods of lifting heavy weights which are least likely to cause a recurrence of symptoms. In cases where acute attacks occur repeatedly, or where the patient complains of chronic backache, radiological examination of the lumbar spine and pelvis should be undertaken to exclude secondary carcinoma, congenital anomalies, caries, osteomyelitis,

unaccompanied by backache. The most important cause of *chronic backache* is degenerative changes in one or more of the intervertebral discs with or without secondary osteoarthritis in the posterior intervertebral articulations Bulging of the annulus or actual protrusion of fragments of the nucleus pulposus may be present without causing pressure on the sciatic roots, but many of these patients eventually develop the signs and symptoms of sciatica (see p 831). Nearly all such cases in the past have been treated as chronic fibrositis of the lumbar muscles. A history of recurrent acute attacks precipitated by sudden move-

the spinal column, a careful search may reveal localized areas of tenderness

SCIATICA

Although sciatica is most commonly due to lesions of the intervertebral discs, it may be a symptom of a number of other conditions. The problem of sciatica and its treatment is dealt with in the section on Neurology (see p. 831).

THE ROLE OF SURGERY IN THE CHRONIC RHEUMATIC DISEASES

Before discussing the part played by surgery in the chronic rheumatic diseases, it must again be emphasized that early and adequate treatment will, in the vast majority of cases, obviate the necessity for surgical intervention. Surgery has no place in the treatment of the acute or subacute stages of rheumatoid arthritis, but offers to an arthritic derelict who has failed to respond to physiotherapeutic measures the only hope of regaining some degree of useful function.

Before surgical measures are considered in the treatment of rheumatoid arthritis, certain criteria must be observed These have been clearly defined by Pemberton and Osgood as follows.

1. Arrest or quiescence of the disease
2. Preliminary treatment to improve the patient's general condition as much as possible.
3. Correct appraisal of the patient as an operative risk.
4. A knowledge of the patient's psychology and a belief in his ability to maintain morale.
5. An accurate estimate of the number and nature of the operations which will be required to attain the functional objective
6. Provision for carrying through the entire operative campaign This includes (*a*) special hospital facilities and optimistic, experienced nursing; (*b*) consideration of the patient's financial resources in relation to after-treatment, especially physical therapy and prolonged "follow-up".
7. Thorough training in joint surgery, good judgment and meticulous technique on the part of the surgeon.

In rheumatoid arthritis deformities requiring surgical correction may be

and time-consuming procedures required for the restoration of the ability to walk.

It is not proposed to give details of the various operations, but merely to *mention the object of each and the type of case on which they can most profitably* be performed.

Synovectomy.—This type of operation is indicated in cases of rheumatoid arthritis and occasionally in cases of menopausal arthritis, *where other forms* of treatment have failed to reduce swelling and disability, and recurrent effusion and pain result from the nipping of tags of proliferated synovial membrane between the articular surfaces. The operation consists in the removal of as much as possible of the hypertrophied synovial membrane in the affected joint.

Capsulotomy.—This operation consists of the division of contracted ligaments and joint capsules which are causing flexion deformities but where a *free range of movement exists up to the position of deformity. It is particularly* applicable to the knee joints, but may be used in other joints.

Arthrotomy.—*In rheumatoid arthritis* an *isolated* mass of proliferated synovial membrane may give rise to disability as a result of being pinched between the articular surfaces during movement of the joint. In osteoarthritis individual chondro-osseous spurs may limit motion, or loose bodies may be present in the joint cavity. In these conditions arthrotomy may be required for their removal. The existence of extensive articular damage is not necessarily a contra-indication to the operation, because relief of acute symptoms may be obtained.

Osteotomy.—*Osteotomy is employed for restoration of the normal align*ment of joint surfaces when a useful range of movement is still present in the joint, or for the correction of mal-alignment in a joint which has already become ankylosed. For example, osteotomy may serve a useful purpose in correcting the flexion and adduction deformities which are common in more advanced cases of osteoarthritis of the hip joint.

Drilling of the Head of the Femur (Forage).—This procedure is no longer employed.

Acetabuloplasty.—In this operation the upper and anterior parts of the acetabular margin are removed because pain on abduction may be due to the con [illegible]
acet [illegible]

[illegible] s
from a functional point of view, considerable benefit may be obtained from a procedure which deprives it of all motion but renders it stable. A joint may still be capable of a limited range of movement but be so painful that from the patient's point of view the movement can be put to no useful purpose. Here, again, artificially produced *ankylosis may* banish pain and enable the patient to use the limb. This type of operation is of value in selected cases of both rheumatoid and osteoarthritis.

[illegible] the bone

[illegible]

Arthroplasty of the hip is a serious operation *from the standpoint* of shock, and many surgeons prefer a McMurray sliding osteotomy. In carefully selected patients with rheumatoid arthritis whose general condition is good, and who will

co-operate willingly in the long post-operative period required to secure a functionally good result, arthroplasty is believed to have a wider application than was hitherto thought. A high degree of surgical skill is essential, and infinite patience on the part of both the surgeon and the patient is required.

cold and clammy. A cervical sympathectomy in the case of the hands and a lumbar sympathectomy in the case of the feet will have the effect of rendering them warm and dry. In early cases some relief of pain and improvement in function may result, but the operations on the sympathetic system have a very limited application in rheumatoid arthritis.

This brief survey of the role of surgery in chronic arthritis may serve to emphasize that the outlook, even in the arthritic derelict, may not be so hopeless as has been previously thought. Success depends upon the close co-operation of physicians and surgeons who have made a special study of the problems presented by the chronic rheumatic diseases

APPENDIX

THE ORGANIZATION OF A RHEUMATISM CLINIC

ing the assumption of a certain degree of independence and responsibility and too often finds himself unequal to the task If the best results are to be obtained

various problems peculiar to the chronic rheumatic diseases. They must visit

It has long been recognized that severe mental shock, profound emotional

ance in patients who, after months or even years in bed, have lost the desire to assume once more the responsibility of independent existence The correction of this mental attitude is essential and requires the most careful consideration of the medical and social service. It is only by close co-operation and prolonged supervision that the full benefit of treatment can be ensured.

METHODS OF APPLYING LOCAL HEAT

Dry Heat.—Salt or sand retains heat for a considerable period and may be used when other methods of applying dry heat are not available. The amount required varies with the part to be treated. Enough must be used to cover completely or enclose the group of muscles or joint affected by the disease. The substance is heated in a metal container over a fire or in an oven and is applied

held fir
which c
and are
trolling
the current is reduced. These pads can be kept in position for two to three hours.

efficient sources of heat. An electric radiator or gas fire can be used if the patient cannot afford a portable lamp, and are satisfactory but not so handy. Exposure to radiant heat or infra-red rays should not exceed fifteen to twenty minutes at a distance of 2 ft. The time of exposure will vary in each individual case, depending on personal sensitivity, and care should be taken particularly with the first two or three exposures to avoid over-exposure, which may cause burns.

Moist Heat.—A simple method of applying moist heat is by means of a mud pack.
substitute fo
pound It
described above. Peat is also employed for this purpose and can be bought in convenient packages for home use Another convenient method of applying local moist heat is the use of a kaolin poultice. The material is packed in tins

three hours.

Paraffin-wax baths.—One of the best methods of applying local heat is by means of paraffin-wax baths The wax can be obtained in bulk from oil merchants or from any pharmacist A double boiler or steamer is used to melt the wax, the melting-point of which is around 100° F. The receptacle should be of sufficient size to permit the immersion of a hand or foot. A large biscuit-tin may serve the purpose When the limb has been immersed, the patient should ... perfectly still for a few seconds or the sensation of heat
... vn and immersed repeatedly, the wax
... each immersion, until five or six coats of wax have been applied. The part is then wrapped up in jaconet and cotton-wool for twenty to thirty minutes The skin perspires freely beneath the wax and a local vapour bath is formed. At the end of the treatment the wax is easily peeled off and leaves an intense erythema of the skin which lasts for some time The wax can be used again and again. This method is very valuable in the treat-

ment of hands and feet of those affected by *rheumatoid arthritis* Pain is eased and movement of the joints is improved. When the affected joint cannot be immersed in the wax (knee, shoulder, etc.), several coats of hot wax are applied by means of a large paint brush, jaconet and cotton-wool being used to retain the heat as before.

Glove Bath.—A method devised by Ray for the local application of heat to the hands or feet has been found to be of service. The hand or foot is covered by a rubber glove or rubber sock several sizes too large and then immersed in water at a temperature of about 110° F for fifteen to twenty [illegible] perspires freely within the rubber covering, pain is relieved [illegible] can be enhanced [illegible] d with the [illegible]

MANUFACTURE OF PLASTER SPLINTS

Wrist Splint.—Soak a plaster of Paris bandage 3 yds long and 4 in. wide in lukewarm water to which a little salt has been added (one to two teaspoonfuls to a basin of water). On a smooth surface (a sheet of thick plate-glass is perhaps the best) make a slab 14 to 16 in. long by rolling the bandage backwards and forwards upon itself. As each successive layer of bandage is added it is rubbed

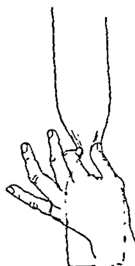


Fig 7—Showing how plaster slab is compressed to form a bar by the forefinger and thumb



Fig 8—Showing the slab moulded into position, short end across the palm and over the dorsum of the hand, long end over dorsum of the hand and up the forearm

smooth with the palm of the hand in order to get rid of air bubbles. When the slab is complete it is grasped firmly with the finger and thumb about 6 in. from one end and compressed into a bar (see Fig 7), which is then placed between the first finger and thumb of the patient's hand, the shorter end of the slab being on the palmar aspect This end is moulded across the patient's palm just

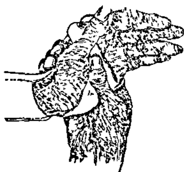


Fig. 9.—Showing how the splint is moulded to hold the wrist in dorsiflexion. Dotted lines on the anterior aspect of the wrist indicate where plaster is to be cut

in dorsiflexion and the transverse palmar arch maintained by pressure of the operator's thumb (see Fig 9) until the plaster has firmly set. The plaster on the anterior aspect of the forearm and wrist is now cut away (see Fig 9) and the splint slipped off. The splint is allowed to dry for twelve hours, after which it can be readily slipped on and off and when in use kept in place by a bandage (preferably crêpe) applied to the forearm. This type of splint is used when the wrist alone is involved. In the acute stage its function is to prevent deformity and secure absolute rest to the joint. In the subacute and chronic stages, where flexion deformity of the wrist already exists, a series of these plasters may be used for its correction, according to the technique described for the knee (see p. 773)

Hand and Wrist Splint.—Make a short slab of plaster bandage 3 to 4 in. wide and 6 to 8 in. long, consisting of six thicknesses of bandage. It is moulded around the fingers and hand. Make a second slab 10 to 12 in long and 4 in. wide, consisting of six to eight thicknesses of bandage. Apply it along the forearm, hand and fingers, overlapping the first slab (see Fig. 10). The two slabs are now fixed together with a plaster bandage While the plaster is still soft, ulnar deviation is corrected, the wrist dorsiflexed and the palmar arch restored. When the plaster is firm, the splint is slipped off and trimmed in order to ensure its easy application and removal. When in use it is held in place by a forearm bandage, as shown in Figs 10 and 11. The splint is used for rest in the acute stage and correction of ulnar deviation and flexion deformity of the wrist in the subacute and chronic stages.

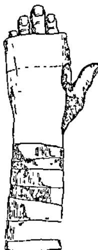


Fig 10—Hand and wrist splint—posterior aspect.



Fig. 11—Hand and wrist splint—anterior aspect.

Rest Splint for Use in the Acute Stage of *Rheumatoid Arthritis*.—For the manufacture of this type of splint a mould is required, consisting of a length

of aluminium 4 in. wide and about 18 in long. It is bent at one end so as to form an eminence upon which the hand rests (see Fig. 12).



Fig 12—Aluminium mould used in manufacture of rest splint for hand and wrist.

The mould is covered with a single layer of stockinet and a plaster slab

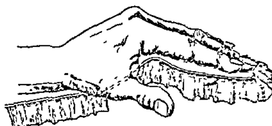


Fig 13—The mould (shown by dotted lines) has been covered with stockinet The hand is resting on the plaster slab. The stockinet is used to mould the slab to the hand and wrist as described

being left free. This has the effect of moulding the plaster firmly to the limb. When the plaster has become set, the splint is removed and trimmed and allowed to dry for twelve hours When in use it is kept bandaged firmly to the hand and arm with a crêpe bandage.

The splints described must be adapted and modified to suit each individual

but in long-standing contractures manipulation under an anæsthetic may be required

POSTURAL, BREATHING AND RE-EDUCATIONAL EXERCISES

For the useful execution of any [illegible]

an exercise:

1. Feet together, looking straight ahead.
2. Knees straight but not tense.
3. Abdomen in, seat down.
4. Rib cage lifted out of waist-line.
5. Shoulder blades pulled gently towards each other, shoulders back and down
6. Arms long and loose by sides.
7. Neck and head pulled back, ears over shoulders.
8. Body-weight slightly forward over toes and outer borders of feet.

The body should feel relaxed To relax does not mean to collapse, but to maintain an effortless balance without strain.

The correct postural position must be checked, and readjusted if necessary, after the performance of each exercise, whether in lying, sitting or standing.

Exercises in Lying

Lying position: On firm support, head, pelvis and feet in line, back flat, hands by sides, feet dorsiflexed.

Abdominal and Breathing Exercises.—*Exercise* 1.—Lying with knees bent. Contract lower abdominal muscles with an inward and upward pull, tighten the buttock muscles, and progressively raise the lumbar then the dorsal spine off the floor. Lower, vertebra by vertebra from the dorsal spine downwards flattening the back against the floor. Relax before repeating. Breathing should be normal.

Exercise 2.—Lying. Bend one knee over the chest, straighten leg and lower, with knee straight. Back, and other leg, should be flat on floor. Repeat alternate.

Exercise 3—Lying, relaxed. Place hands on either side of lower chest wall. Keeping back flat, breathe in slowly, expanding the ribs outwards into the hands Hold breath for a moment, then exhale slowly through the mouth, *allowing ribs to collapse inwards.* Repeat

Exercise 4—Repeat above, but reinforce the expiration by drawing the abdominal muscles in and up. Relax all muscles and tension before breathing in again.

Arm, Shoulder and Neck Exercises.—*Exercise* 5.—Lying. Lightly clasp the hands in front. Raise both arms overhead, stretch tall. Separate hands, and pulling shoulder blades firmly together, lower arms sideways against the floor, completing a circle. Repeat.

Exercise 6.—Lying Raise arms sideways to shoulder level, palms upward. Press arms and head firmly against floor, chin in, and raise upper back off floor. Relax and lower arms to sides Repeat

Exercise 7.—Lying. Turn head side to side. Alternate.

Exercise 8.—Bend towards shoulder. Alternate.

Exercises in Sitting

Sitting posture: Thighs and buttocks should be supported on stool of correct height. Knees and feet together. Body as described for standing posture.

Shoulder and Trunk Exercises.—*Exercise* 9—Postural correction. Relax body forward, chin on chest, back rounded, arms and hands hanging [illegible]

feeling of relaxation should still be present with the arms long and loose. Repeat between exercises.

Exercise 10.—Repeat exercise 5 in the sitting position.

Exercise 11—Swing arms loosely forwards and upwards overhead, then back. Repeat

Exercise 12—Clap hands sideways overhead, and drop to sides again. Repeat.

Exercise 13 Using ball or other object, pass this from the right hand behind the neck to the left hand, and then behind back to the right hand Repeat and alternate

Exercise 14—Sitting, feet and knees apart, hands on hips Bend upper part of trunk to side, alternate.

Exercise 15—Position as above Turn trunk to side, alternate

Exercises in Standing

Exercise 16—Postural correction Stand against wall, head, shoulders and hips against wall, chin and abdomen in Stretch tall without strain. Walk forward retaining correct posture Repeat

Exercise 17.—Following above exercise, walk along a straight line keeping feet straight, and using heel-to-toe leverage.

Exercise 18.—Standing, feet straight and 4 to 6 in apart, hands on hips. Repeat exercises 14 and 15 Avoid sway of pelvis or ankles.

Exercise 19—Standing Inhale, raising arms sideways and upwards, rise on toes and stretch tall As heels sink, lower arms to sides and exhale, drawing abdomen in.

Foot Exercises

Exercises to correct faulty body mechanics should always include training in the proper use of the feet It should be remembered that when a muscle is used in the right way it becomes stronger, and therefore before any foot exercises are given the patient should be shown how to use the feet properly The correct standing position must begin with the position of the feet in weight bearing. The feet should be comfortably straight ahead with the weight on the outer border, toes on the ground. Use of the feet in this position means correct use of all the foot muscles.

Exercise 1.—Sitting, cross knees Make half circle with foot, down, in and up The inward, upward pull is the important result.

Exercise 2.—Same position, turn foot in *slightly*. Pull foot up and push down, using ankle joint.

Exercise 3.—Same position. Turn foot in, curl toes under hard. Pull foot up when toes are curled.

Exercise 4.—Standing, weight well forward, body in good line, hands on hips. Lift inner borders of feet, relax half-way and repeat. Toes cling to floor.

Exercise 5.—Same position. Lift inner borders of feet, rock from heel to toe. Do not let inner border of feet down.

Exercise 6.—Heel-and-toe walk on line. Described in previous list.

Exercise 7.—Sitting. Pick up marbles with toes, turn foot up, and hand to yourself.

Exercise 8.—Sitting. Place bath towel, folded full length, on floor; using toes and outer border of foot, draw whole length of the towel towards you. Do not let heel move out of position or rest on towel.

Hand Exercises (*Active*)

Starting Position.—Sitting at a table with the forearm at a right angle and supinated to mid-position.

Exercises to Enable Patient to Flex Fingers.—1. Flexion of each joint of the fingers separately into the palm of hand, assisted by other hand or operator.

2 Place a small rubber ball into the palm and tell patient to alternately "squeeze and release". This may be made more difficult by using a soft piece of sponge.

Exercises to Overcome Flexion Deformity.—1. Placing the hand as flat as possible on the table and with the forearm fixed stretch the fingers forward as far as possible.

2. Stretching fingers and lifting each up off the table separately.

Exercises to Obtain Extension of Wrist.—1*. Forearm supinated, hand over edge of table, wrist extension.

Same exercise may be performed with gravity eliminated, i.e. with forearm in mid-position; or gravity resisting, i.e. forearm pronated.

2. Place forearm on table, palm downwards; raise forearm up, keeping hand fixed.

3. Wringing a duster.

4. Climbing up the wall bars.

Exercises to Obtain Flexion of Wrist.—Same as 1*, except the arm is pronated in the first part of exercise and the wrist is moved to the flexed position.

Other Exercises.

1. Stretching the fingers upon the table, separate them as far as possible. If adduction is limited, adduct each finger separately to the middle line of the hand.

2. Forearm supinated, flex the thumb into the palm of the hand.

3. In same position oppose thumb to little finger.

4 With wrists extended and resting on edge of table, perform movements with fingers as if playing piano, taking care not to produce *ulnar deviation*

5. Picking up objects (large ones to commence with) such as a reel of

This may be progressed by

DETERMINATION OF THE SEDIMENTATION RATE

The test measures the rate of fall of the blood corpuscles in a perpendicular column of blood maintained at room temperature (65° F.). To obtain accurate readings an elaborate technique is required. General practitioners have neither the time nor the apparatus for carrying out such a procedure, but the method described below is sufficiently accurate for practical purposes

The test is not diagnostic of any particular disease, since an increased sedimentation rate is found in all infections. In a healthy person the sedimentation rate is between 5 and 15 mm in an hour. In the acute stage of rheumatoid arthritis the one-hour reading may be 80 to 100 mm or even more. When the activity abates as a result of treatment, or during a natural remission of the disease, the rate decreases, but any intercurrent infection such as a common

after the withdrawal of the blood and certainly within three hours The

cytes is noted at the end of one hour

DISEASES OF BONE

The following diseases of bone have been discussed in other sections: rickets on p 341, osteomalacia (mollities ossium) on p. 342, osteitis fibrosa cystica (von Recklinghausen's disease) on p 371, multiple myeloma (myeloma-

There remain certain uncommon diseases of bone for which no specific medical treatment is available, namely achondroplasia, hypertrophic pulmonary osteoarthropathy, osteitis deformans (Paget's disease), leontiasis ossea, oxycephaly and osteogenesis imperfecta (fragilitas ossium)

L. S. P. DAVIDSON.
J. J. R. DUTHIE.

PSYCHOTHERAPY IN GENERAL PRACTICE

INTRODUCTION

UNTIL RECENTLY the teaching of psychiatry at most medical schools was largely restricted to the diagnosis of the psychoses, and it is notorious that all that most doctors remember of their undergraduate instruction is the demonstration of patients at the local mental hospital It was presumably because of this misplaced emphasis that so many doctors used to believe that psychiatry and psychology were concerned only with abnormal persons whose minds were in some way deranged. Few doctors, or for that

are emotional and psychological; and as a corollary to this that in all illnesses which are not purely psychological, psychotherapy is inappropriate and physical treatment alone should be used.

These misunderstandings stem from the persistent idea that mind and body are two separate entities; the one, immaterial, elusive and defying scientific study is something to be dealt with only by priests, quacks and the more eccentric members of the profession; the other, solid and predictable, accessible to physical, chemical and microscopic investigation, is a respectable subject for investigation by scientific medical men

The modern view regards mind and body as two aspects of one unity, the human organism, and this conception is more in accord with the facts. Psychological and physiological processes interact on one another and parallel each other; the thought of danger and the feeling of fear are accompanied by changes in heart beat and blood chemistry, while conversely alcohol or the toxins of disease affect thought and feeling.

The terms psychological and physiological refer to different levels of function. When we are dealing with variations in the function of an *organ*, it is appropriate to think in terms of physics or chemistry (as, for example, when

something about the emotions of the patient, but it is conversely true that the *thoughts and feelings of the patient may help to explain the physical findings*

In practice, unless we are morbid anatomists, we are not dealing with organs but with patients, and no doctor, unless he is extremely naïve and inexperienced, does in fact think of a patient in terms of the various systems as set out in a *scheme of physical examination; he recognizes these as abstractions* which he makes to order his observations and facilitate diagnosis.

The experienced doctor is constantly aware of and treats psychological effects in all kinds of illness, even in the infectious fevers where, although the *physical findings may follow* a standard pattern, the patient's emotional response and consequently the real significance of the illness to him will be

determined by his personality, his responsibilities and his social environment. Health and disease are manifestations of a complex process of adjustment to many factors both internal and external, and what the patient thinks and feels is never entirely irrelevant and may often be crucial to the understanding of illness [illegible]

accord with facts and give meaning and order to clinical observations in the neuroses. We know now that the symptoms of the neuroses are not haphazard, incoherent and irrational, but that with patience they are capable of being completely understood and their sources identified We have gained insight into the development of personality and the effects of parental care and upbringing and we have learned that many of our conflicts take place below the level of consciousness We have come to look for an understanding of a neurosis in the life-history of the patient, in the cultural influences to which he has been exposed and in the current emotional stresses which he is facing.

But our understanding of psychological factors in disease has by no means been due entirely to the work of psychiatrists, it has emerged also from clinical studies and research within general medicine. Success in dealing with noxious factors in the environment characterized the first sanitary phase of modern medicine, and then followed the great advances in immunotherapy, chemotherapy and the correction of hormone and vitamin insufficiencies These discoveries gave a satisfactory explanation of the ætiology of the majority of diseases, but some remain, as the textbooks say, " of indefinite or unknown pathology " A number of the latter conditions have recently been called " stress diseases " or " psychosomatic disorders " because the general adaptation of the individual appears to play a part, and emotional as well as physical factors are considered to be relevant to their ætiology.

It has been noticed and confirmed in more than one country that stress diseases and the psychoneuroses are showing a very great increase in incidence The observation that the increase has occurred only in industrialized communities with a complex and rapidly changing environment seems to confirm the view that difficulty in adaptation is a factor in these illnesses Specific environmental causes, however, have not yet been identified. Many believe that [illegible]

attain prescribed standards of proficiency—and equally those who repudiate such formulæ—are beset with psychological problems which they must try to resolve, because the individual can never escape from the awareness that he is constantly being judged by the herd or " community ".

will lose the feeling of security which comes from being able to approach someone who is himself secure and stands outside of his difficulties But he must feel that his physician has a human interest in him and can give him emotional understanding. To strike the right balance between over-detachment and over-involvement is the main problem of the doctor-patient relationship; fortunately, the conscientious doctor who tries to serve all his patients without favouritism is likely to arrive at an attitude which is more or less appropriate. To lessen the blow of our failures and the impact of everyday tragedies we doctors sometimes imagine ourselves as automata who have become impervious to the emotional effects of our calling, but what progress we make in this direction is but partial and it is as well to recognize that complete detachment would not, in fact, be conducive to therapeutic success

Emotional dependence is not difficult to endure when it is positive. It is easy to like and appreciate and do our best for patients who like us and show us respect, but we should contrive also to give of our best to those who are negative towards us Positive and negative attitudes expressed towards the doctor are usually not personal attitudes expressed towards him as a real person, but accrue to him in his capacity as a symbolic figure In other words, it is helpful to realize that the doctor does not usually earn the negative feelings which some patients display towards him even if it is salutary for him to remember that positive feelings and respect are often equally unmerited and unreasonable.

Transference acts in two directions and the doctor has to be alive to his own emotional response to a patient's display of respect and affection. A likeable dependent patient should be saved from over-dependence and continued invalidism even at the risk of the doctor falling somewhat in the patient's regard.

When the patient is negative that attitude can be challenged too, and the doctor should ask—not aggressively but in a way which the patient realizes is intended to increase the doctor's understanding of his problems—why he appears hostile and unco-operative. The doctor must be prepared to hear a few home truths and to accept them in unruffled fashion, but the upshot may well be and usually is a reduction of hostility, increased co-operation, and the realization that what the patient has expressed had very little to do with what the doctor had actually done.

The doctor should strive to recognize his own blind-spots and prejudices. Psychotherapists nowadays undergo a personal analysis in order to gain this insight. However, if the doctor consistently tries to avoid a moralistic and critical attitude he will not only learn a good deal about his patients but in course of time he will come to learn a good deal about himself.

THE INTERVIEW

Theory.—Psychotherapy is carried out mainly by means of the interview. How a psychiatric interview is conducted is determined by what is known about the ætiology of the neuroses.

It is useful, for example, to remember that neurotic symptoms have a [illegible] much the same way as physical symptoms like pain, [illegible] ey are warnings of things [illegible] Pain is physical unease, and for its psychic analogue, mental unease, we use the term *anxiety* Anxiety

occurs whenever there is a threat to the functioning of the organism; if it comes from without, the anxiety has the character of fear, whereas when the danger threatens from within, in a conflict between desire and conscience, it may have the quality of worry, guilt or remorse depending on the precise internal situation which creates the anxiety. Anxiety is the commonest symptom of neurosis, and many other neurotic symptoms arise out of it as means of avoiding, dispelling or absorbing anxiety. In the healthy person anxiety can be removed by taking appropriate action unless, as sometimes happens, there is no escape from the situation which provokes it. When, however, anxiety is neurotic there is either no obvious situation to which the individual is responding or his reaction to the situation is inappropriate or out of proportion to the threat it holds for him. But there is no hard and fast line between neurotic and normal anxiety. Emotional situations always stir up reverberations from similar situations in earlier life, so that emotional reactions are seldom, even in the healthy person, entirely appropriate to the circumstances which arouse them.

lengthy psychotherapeutic procedures of an analytic or uncovering type that neurotic anxiety arises from repressed infantile situations which are touched off by current happenings, the connection being unrecognized by the patient.

is important to review the patient's emotional reactions and to seek such characteristic patterns. By discussing these patterns of behaviour the patient will achieve emotional insight It is not enough for the doctor to perceive the neurotic

good personal relationship has been established between doctor and patient.

When anxiety shows itself, quite irrationally, in certain situations in which there is no apparent danger, as is seen very commonly in *phobias* of closed places such as cinemas or churches, we are usually dealing with a very deep-seated source of anxiety
although the patient can
Here the danger arises fr

outwards to specific situations in the form of a phobia allows the patient to deal with it by avoidance as if it were an external danger.

In *hysteria* the typical symptom is one of a physical disturbance without physical disease. The symptom is an attempt to solve an emotional conflict by translating it into physical terms and so reducing anxiety.

> A middle-aged woman, attempting to carry out her mother's unreasonable death-bed command and thereby finding herself in serious conflict with her husband and children, solved her problem by developing a paralysis of her legs which restored the concern and attention of her family while it prevented her from obeying her mother's command.

The hysteric by exploiting this mechanism often succeeds in avoiding anxiety altogether, presenting a picture of smiling indifference in spite of severe disability. This evasion of anxiety is fundamental to the personality of hysterics.

Since neurotic symptoms arise out of and have relevance to enduring traits in the personality, an important part of the life-history interview both for diagnosis and treatment lies in an assessment of personality and an understanding of its dynamics. Hysterics, for example, are often impressive characters, sure of their own virtues and superior to the failings of others, skilful in manipulating the emotions of those around them—sometimes even including those of the doctor—and contriving always to present themselves in the best possible light. Their spite and revengefulness may be perceived only by their few immediate victims who often prefer to remain silent, doubting their own judgment and blaming themselves, rather than challenge the good opinion held by others. When the doctor listens to a life-history in which there are few shortcomings and which seems to be unusually devoid of blame, this in itself ... life-pattern of hysterical patients

... recognized from the life-history even in the absence of overt manifestations of the obsessive-compulsive neurosis. The following traits can be regarded as typical although the obsessional personality is extremely variable. There is obvious concern about the control of the inanimate environment with emphasis on orderliness, cleanliness, neatness and method. There is scrupulous attention to detail: obligations involving the welfare of other people are discharged with meticulous care. In human relationships there is an ill-concealed desire for power and a fear of losing self-esteem. Justice and fair play are of special emotional significance, but underlying these attitudes there are concealed aggressive trends towards significant persons. Ambivalence towards love objects is a special problem for obsessionals and is seen in the difficulty and indecision they may show in the choosing of a marital partner. Interest in vague humanitarian conceptions implying altruism and ...

lated into somatic dysfunction may arise from an inability to express freely emotions of love or hostility.

It is true to say that all neuroses have their roots in disturbances of ...al relationships whether we are considering the early primary family

relationships or the traumatic situations of adult life which precipitate the neurosis. Even in the extreme case of the war neurosis there is not only fear of

brothers and sisters. The ways in which he adjusts to the family, the first group of which he is a member, modify and characterize his relations with those he meets in all later groups, and insight into this fact is an important aim in therapy. Of these early relationships the relationship with the mother is most crucial for emotional development. Later feelings of insecurity and incapacity in forming affectionate relationships often appear to arise from separation from the mother in infancy or from attitudes or rejection on her part which deny the child the experience of a warm affection. During the remainder of his life he may con-

He has shown its origin in separation from the mother in infancy and its effects in later life in behaviour characterized by delinquency.

Procedure.—To start the patient talking he should be asked about his *complaints* and everything he says should be carefully noted. In considering these complaints the doctor should make due allowance for the patient's tendency to minimize the expression of emotion while emphasizing any somatic disturbance which he experiences; if the patient does try to describe his tension or his feelings of anxiety, he should be encouraged to expand his description. No attempt should be made to switch the patient away from his complaints until the doctor is satisfied that he fully understands them.

insurance and compensation may provide relevant data.

When the history of the illness has been brought up to the present, the interview should go on to take account of the patient's *life-history*. It is necessary to get to know the patient as a person, and this aim can be conveyed by asking "Where were you born and brought up? Where do you come in the family?" If the patient begins to talk of the family situation and his early relationships with his parents, so much the better, but, at this stage in a first interview, direct questioning about sibling rivalry, attitude to parents or parental attitudes to the patient, may arouse resentment and should be avoided. It is better to come back to these points later when the patient has gained confidence and through discussion of his contemporary situation has developed insight into his basic emotional attitudes.

The usual medical inquiries about illnesses in childhood should precede questions about nervousness and childhood fears, which should be made as concrete as possible as, for example: "Most children fear the dark; did you have any special fears of that kind? How did you get on at school? Did you have any special worries about your school work? How did you get on with your teachers?" Such inquiries may lead the patient to describe other significant fears or upsets related to his family.

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It is true to say that all neuroses have their roots in disturbances of [illegible] relationships whether we are considering the early primary family

relationships or the traumatic situations of adult life which precipitate the neurosis. Even in the extreme case of the war neurosis there is not only fear of [illegible]

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The age of the patient at the time of the death of a parent or a near relative should be carefully noted along with any indications of emotional disturbance related to the death. The sequence of events is specially important and questions should be put so that any relationship between significant events and developments in the *life situation of the patient is clearly established.*

It is important to assess the patient's intelligence and the best indicator is usually the school record. A careful note should be taken of the ages at which the various educational levels were achieved.

The work record often provides clues to personality difficulties in the reasons given for leaving a job or for choosing a new occupation. It is also important to inquire into the patient's prospects of promotion and any disappointments he has suffered in this respect. The importance of sexual experience in determining psychological attitudes should not be forgotten, and some attention should be devoted to the sex life of the patient

It is possible in a first interview to ask questions about the sex life, but these should be factual and more or less confined to such conventional inquiries as the patient would expect from the doctor. He can be asked about courtship
when he married, and the number
about marital relations should be
obviously forthcoming and wishes to talk, as he usually will when there is marital discord and overt emotional stress. Women patients usually talk more readily about their sex life than do men and are more apt to grasp the significance of the doctor's inquiries in this field.

Questions about the financial position of the household, housing difficulties, relationship with in-laws, etc, are often of special importance, and the doctor should satisfy himself that he has a clear picture of the patient as he now lives in respect to his family situation, work, friends and recreation.

Personality is best assessed by considering the life-history and the clues which the patient gives in the interview, the things he stresses and his attitude towards the doctor; often, too, his mannerisms and his emotional reactions to specific topics are informative. Some inquiries can be made directly; for example, his sociability can be assessed by questions regarding his leisure-time pursuits, whether he seeks the company of others or prefers a solitary hobby. Knowledge of his habits and likes and dislikes may indicate the unduly methodical personality of the obsessional which in turn may suggest further investigation into his relationships with others.

In taking the *family history*, it is as well to avoid too direct inquiries into the presence or absence of mental illness in the family. Patients suffering from neurosis are often afraid of insanity, and if the doctor makes a special point of this question it will suggest to the patient that the doctor suspects that he is liable to become insane *The chief importance of a family history of mental* illness is, in any case, not the hereditary factor but the effect it has had on the patient's upbringing, and this should emerge incidentally in the account that the patient gives of his life-history.

In all cases the doctor should carry out a careful *physical examination* and, in doing so, he should remember the neurotic fears which the patient may have and the need to reassure him. If he finds it necessary to linger over the auscultation of an area in the chest, he should remember the consequent fear that may arise in the patient's mind and try to allay it immediately. He should keep to himself any doubts he may have and so avoid implanting the

idea—widespread among neurotic patients—that they are puzzling cases of physical illness.

When he has covered the life-history and made a physical examination, the doctor should be in a position to decide whether the patient is suffering from a neurosis or whether the diagnosis needs to be completed by special investigations such as X-ray of skull, blood and C.S F. examination, electro-encephalography or examination by a specialist. If the doctor has no reasonable doubt, and especially if he has positive findings of an emotional disturbance to account for the patient's complaints—which will usually be the case—he

enough to prevent the patient from gaining the impression that the doctor is accusing him of malingering or of having imaginary pains, and this may involve giving the patient a simple account of how emotions may produce bodily disturbance. For instance, if the patient has pain and stiffness in muscles, the doctor can point out that heightened emotion is often accompanied by a tense bodily state and that this could account for his symptoms The patient can also be made to understand how headache, tachycardia, nausea, diarrhœa or constipation can be produced in a like manner

An interview such as has been described, especially if it has given the patient an opportunity to vent his emotions, has in itself great therapeutic value. It will be noticed that the doctor has been called upon to do little more than adopt the attitude of an interested listener and no interpretation of the patient's emotional attitudes has necessarily been undertaken Premature interpretation and reassurance have to be avoided, there is usually resistance on the part of the patient to gaining insight into his own emotions, and he therefore discloses his fears and his guilt only by instalments If the doctor rushes in with an interpretation of the patient's attitudes before they are fully disclosed, it will diminish the patient's confidence in the doctor's wisdom and will effectively block, at least for a time, any further disclosure which he had been willing to make The patient may well react negatively in such a situation and the doctor may become aware of his hostility. He should take it in an unruffled fashion which will effectively reassure the patient and reduce his resistance, because it will have demonstrated to him that the doctor accepts him for what he is, good and bad together, and that the doctor's aim is to understand how he has become what he is and not to sit in judgment on him

Each interview will leave some questions unanswered and suggest topics for further interviews This material should be noted and raised again when a suitable opportunity occurs

PATIENTS REQUIRING A SPECIALIST OPINION

Many psychiatric patients require to be referred to a trained psychiatrist for

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done, the patient may be resentful and suspicious towards his doctor and hostile and unco-operative to the psychiatrist. This can happen even when the patient himself has already come to the conclusion that he should see a psychiatrist. His objection arises from the fact that he suspects he is being sent for the wrong reason; he may believe that the doctor thinks he is going insane or that he is malingering. In referring the patient, an adequate history is of the greatest help. If the doctor has already been taken into the patient's confidence and knows his patient's intimate problem, he should obtain his consent to include this information in the letter of introduction, which will save the patient the embarrassment of having to break into the subject himself and will smooth the process of communicating the history to the specialist.

The specialist's advice will take the form of recommending how the practitioner can continue to treat the patient or he may advise treatment in hospital [illegible] elsewhere. The doctor's duty in such a case is to try to persuade the patient to [illegible] end falling into the clutches of the quack.

The closer the practitioner works with the psychiatrist the better, and he should try to know him personally so that informal exchanges on the telephone [illegible] The doctor should not hesitate [illegible] be available to help patients. [illegible] hiatrist should have a special knowledge of such facilities and the doctor should profit from his knowledge so that he himself can make the best use of all the services and agencies which are available.

Certain groups of patients will almost always have to be referred to specialist facilities.

For example, *acute psychotic patients* cannot as a rule be handled in general practice and the doctor's main duty is early recognition. In such cases the relatives will emphasize the change in behaviour and personality which indicates not the part-reaction of the neurosis, in which the personality is preserved, but the whole-reaction of the psychosis, where the personality change is conspicuous. Seclusiveness, bizarre behaviour and utterances, grotesque hypochondriacal [illegible] best to influence the patient's relatives to follow this advice.

Sometimes the patient suffering from a psychosis is seen as an acute emergency in a state of great restlessness or excitement, and the problem is one of rapid sedation. In these circumstances the most effective method is to administer hyoscine hydrobromide, 1 mg ($\frac{1}{60}$ gr.), hypodermically or intramuscularly, or an injection containing morphine, 15 mg. ($\frac{1}{4}$ gr.), and hyoscine, 0.5 mg. ($\frac{1}{120}$ gr.).

A decision as to what to do with a patient who complains of *acute depression* presents a special problem and something needs to be said about the factors which should be taken into account. The doctor will wish to know whether

[illegible]

and exposure, and consequently a number of would-be suicides do not regard themselves as being ill and do not seek a doctor's help. But while it is statistically true that suicide is frequent in the absence of a complaint of psychiatric illness, the risk of suicide is always to be taken seriously when a patient does complain of depression. Unfortunately there are no precise criteria by which the danger of suicide can be judged, but there are some guiding principles which will help the doctor in forming an opinion. The first guide is to be found in the diagnosis. Patients can be divided into three groups:

1. Those suffering from endogenous psychoses (the depressive phase of the manic-depressive psychosis, and involutional melancholia).
2. The reactive depressions in which the depression is clearly connected [illegible] illness such as an anxiety neurosis, hysteria or obsessional state.
3. Depressive reactions occurring in organic conditions such as G P.I., locomotor ataxia, arteriosclerotic brain disease or brain tumour.

[illegible]

a patient suffering from manic-depressive psychosis committed suicide by thrusting a red-hot poker down her throat. Some patients never relent in their desire for self-destruction, and by sheer cunning they succeed even when the greatest care is taken under mental hospital conditions.

[illegible]

and of things around him appearing to be different. When [illegible]

of the severity of the depression are to be found in the somatic symptoms; severe insomnia, loss of appetite, constipation and loss of weight all point to a dangerous condition.

If the practitioner has come to the conclusion that the patient is seriously [illegible]

not worth living, he can usually be asked whether he has contemplated suicide and he may well give an accurate account of any such preoccupations The common belief that those who talk of suicide never carry out their threat is quite untrue, although, of course, there are patients who talk glibly about suicide without having any suicidal intention. Most patients who do commit suicide have usually mentioned their intention to someone.

In the reactive depressions the danger of suicide is less easy to gauge. If depression is constant and is maintained unrelieved for days or weeks at a time, the danger of suicide is greater. But in many cases, although the patient complains of depression, he experiences it at most only for a day or two at a time and in the intervals his spirits are normal; in these cases the danger of suicide is much less. In addition, in the reactive depression there is a need to estimate the gravity of the external situation and the possibility that the patient may respond to a serious dilemma by attempting suicide. Occasionally it is advisable to recommend a patient for admission to a psychiatric unit even when his response appears to be a normal one.

A young man had started a business and had received advances of capital from several friends. Owing to the defalcations of a partner the money had been lost. In the face of this situation the patient was contemplating suicide. He agreed to come into a psychiatric unit and after a short time he was discharged able to face the situation in a more realistic way.

Generally speaking, the more intense the depression the more likely it is to [illegible] doubt about [illegible] ing not only [illegible] likely to be effective.

The much commoner minor degrees of depression necessarily fall to be treated by the practitioner and are dealt with later [illegible] characterized in the acute reactions by delirium and [illegible] personality and loss [illegible] due to an infection or alcohol the duration of the illness is likely to be short and the patient should be admitted to a nursing home or a general hospital rather than to a mental hospital. Organic brain disease should be considered as a possibility when any patient over the age of forty, in the absence of great stress, develops neurotic symptoms for the first time; it was mentioned above that depression may be [illegible]

If the practitioner has reason to believe that a young child is suffering from serious *mental deficiency*, he should advise that the child should be taken to a psychiatrist as early as possible. It sometimes seems kinder to wait for a time

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If the practitioner's psychotherapy is to be effective and rewarding, he must try to avoid undertaking the treatment of those *deep-seated neuroses* which require techniques beyond his scope. In deciding what treatment the patient requires he should bear in mind the following rough guides.

1. Acute neuroses respond more readily than chronic neuroses.
2. Neuroses which arise in a clearly traumatic way, for example, from an accident or an intolerable life situation, are of better prognosis than those which occur without any obvious cause
3. Anxiety states with marked phobias (fear of closed spaces, fear of being out alone, etc) are more difficult to treat than those in which the anxiety is unrelated to specific situations
4. Obsessional neuroses, which are usually very chronic, are notoriously ... even by the most expert and lengthy pro-
5. Patients suffering from neuroses in which ... disorder or in whom there is a psychotic element, for example, morbid suspicion, are not good subjects for psychotherapy.
6. W... hysterical symptoms arise out of severe acute anxiety states, for ... loss of speech and ... he prognosis is good. Generally, however, ... the symptoms are exploited to deal with long-term emotional difficulties, only the most intense and lengthy treatment is likely to be effective. The success of superficial procedures, e.g suggestion, hypnotism, etc, in temporarily removing a symptom is no indication that the underlying condition is significantly affected

Most *sexual maladjustments* seen by the practitioner are of a kind in which his therapy is likely to be effective. There are others, however, which require lengthy investigative techniques if, indeed, they can be treated at all

Homosexuality, which is accepted by the patient, and which he does not desire to change, will probably be unaffected by treatment; it is for the practitioner to advise the patient to this effect and to give him what support he can in coming to an adjustment which will enable him to avoid anti-social activity. ... however, more prone to suffer from neurosis than those with ... referred to the psychiatrist. ... ification and excitement are ... bjects, for example, women's ... ot, etc.

... ratification is associated with ... are sexual deviations which should always be referred to ... ists and those who suffer from

transvestitism are prone to overwhelming attacks of anxiety and depression which may lead to suicide, and since they are likely to complain to the doctor only when their anxiety becomes great, this danger should be recognized.

Nowadays child guidance or child psychiatry clinics are available in many places for the treatment of *children with behaviour disorders.* When the disturbance constitutes more than a passing phase in development it is probably better to refer the child for treatment at one of these centres. Minor disturbances are discussed below.

PSYCHOTHERAPEUTIC TASKS WITHIN THE SCOPE OF THE GENERAL PRACTITIONER

Mild Depressions.—In the previous section the importance of recognizing the more severe states of depression was emphasized. There are other patients who either complain of mild depression or who may present themselves with minor physical complaints. Not all of these need specialist treatment. Indeed, depression arising out of modern stresses is among the commonest of *all complaints, and for this the general practitioner can do a great deal.* The patient will often feel a need to unburden himself about his disappointments, his frustrations and his sense of failure. This need not be a lengthy affair, and if the symptoms seem clearly to be those of a minor depressive reaction, not *interfering noticeably with work or concentration or leisure-time pursuits, the* doctor can proceed to reassure the patient. The patient may require to be taken in hand and helped to organize his work and his leisure in such a way that he obtains more satisfaction from them Occupational therapy is useful, and in general practice this may amount to advice on a hobby, taking into account the patient's personality and previous interests.

If he is sleeping less soundly than usual the patient should be given a hypnotic. For this purpose the practitioner should not be reluctant to use sodium barbitone, 0 3 to 0 5 g. (5 to 7½ gr). The slight continuance of the effect noticeable after waking is usually no disadvantage to the patient, who is apt to feel anxious and depressed when he first faces the cares of the day. Chloral hydrate, 1·3 to 2 g. (20 to 30 gr.), well diluted with water, flavoured with syrup or orange, is a reliable and harmless sedative. Phenobarbitone should be avoided because in some patients a hypnotic effect is not obtained, except with an unduly large dose. The newer, more rapidly acting barbiturates should, if prescribed at all for psychiatric patients in practice, be used only for very short periods and in small dosage because they can produce habituation *and addiction and a troublesome withdrawal syndrome.*

[illegible] to keep in frequent touch with the mildly depressed [illegible] of [illegible] sion develop.

Patients with Slight Mental Defect.—Patients who are mentally inadequate, but not sufficiently to be classed as mental defectives, constitute a largely unrecognized psychiatric problem. They are specially prone to psychiatric disorders of all kinds, psychoneuroses, psychoses, sexual deviations and delinquency. Although, because of their inadequate intelligence, they are unable to co-operate in formal psychotherapy, their neurosis is often less deep-rooted than in more intelligent patients so that they respond to simpler therapeutic aid.

The main problem of their lives lies in the extreme difficulty which they experience in coping with tasks which are well within the powers of the average person. This was seen in their reaction to military training. When subjected

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important. The job should be within the ... and the employer should be understanding In larger concerns the patient may become the butt of his workmates, in smaller groups protective attitudes are more likely to be developed towards him. The doctor should seek the help of social service agencies and official personnel officers in dealing with these problems. Often the patient prospers if a social worker makes a good contact with him and his family and the patient knows he can readily turn to her whenever he is in a difficulty.

Childhood Problems.—*Concern about the behaviour problems of children has become so earnest and so fashionable that the slightest deviation is apt nowadays to give rise to serious anxiety on the part of the parents The effect of parental behaviour in developing personality probably needed emphasizing, but the lesson has been so well learned that parents are too ready to feel guilty and over-anxious. Usually all that is required is normal warm affection and tolerance.*

Since many problems of childhood are transient, the doctor's task is often to ensure that the parents do not take too serious a view of the child's deviation and are able to treat him with understanding and patience. It has been said that there are no " problem children ", only problem parents, which is largely,

Problem parents have often had difficult childhood

mon sense support and advice from the doctor ...

of great service It is well to remember also that there are inevitable conflicts and anxieties connected with growing up and surrendering instinctual gratifica-

the power of the parents

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cannot be reared in a state of nature ... to certain social conventions

A view propagated by authorities a generation ago is still held by some mothers who believe it is possible to train a child in sphincter control from the earliest months. It is possible to achieve a brief and spurious success at the age of six months or even earlier by placing the child on the pot soon after he has been fed. The mother's pride in this achievement is soon dashed when after a short time the inevitable failure occurs. These failures tend to be regarded as naughtiness, and the mother persists in her efforts at training but with heightened emotion and greater determination. Antagonistic reactions usually

the pot but gives way

avoided if parents are made to realize that the child is not equipped, neurologically or psychologically, to respond to habit training until he is well into his second year, and that occasional failures are normal and to be expected for another year at least

For her convenience alone, a mother may begin to place a baby on the pot at eight or nine months and, by careful strategy based on observation of the rhythm of the child's activities, benefit from the reflex activity which occurs after feeding or after waking up from sleep, but she should not deceive herself into believing that she is likely to succeed in permanently solving the problem at this stage. It is important to deal with the anxiety of parents in regard to sphincter training, because, if they believe that they are failing or that the child is playing up, they may respond by punishment which is likely to make things worse. A severe attitude on the part of parents during habit training, producing anxiety in the child, is a common cause of bowel incontinence (encopresis) in later infancy The state of anxiety and insecurity which a child may experience on the arrival of a new baby, when he has to take second place, may cause a regression to infantile behaviour and soiling so that he can obtain more of his mother's attention A simple explanation of the emotional reasons for the child's failing, which avoids blaming the mother who is probably already over-anxious, is the correct line of treatment. If soiling occurs in children of school age, however, this is evidence of a severe maladjustment for which the child should be referred to a clinic.

Constipation in young children in the absence of physical causes is more often a symptom of maternal anxiety than of an emotional disturbance on the child's part. The mother who complains of the child's constipation is usually one who has been brought up to believe that there is something wrong if the bowels do not move with absolute regularity. They have usually had recourse to enemas, suppositories and laxatives before consulting the doctor. Again it is the mother who requires re-education and emotional understanding.

What has been said of encopresis is true also of enuresis ; over-anxiety and, in a few cases, parental neglect and carelessness, are the chief causes. Control of the bladder is not usually achieved until the child is well into his second year and, again, accidents are frequent for the next year or so, especially in boys. By the time a child is established as a bed-wetter there is usually already a long history of parental nagging, scolding, punishment and shaming, and the child has come to regard himself as wicked or very abnormal. The doctor has to handle the parents very carefully to obtain all the co-operation he can from them. It is usually difficult for them to give up the punitive and hostile attitudes which they have developed towards the child. they may look upon themselves as being morally in the right and believe that they punish the child more in sorrow than in anger. The best results are often achieved by the doctor assuming the role of the good parent , adopting a permissive attitude to counterbalance the parent's severity, reassuring the child that he is not bad and promising to see

...port progress.

...ct of parental anxiety and over-

...n early infancy when the mother interprets too literally and too slavishly the amount of milk prescribed in the baby-book and a struggle commences to make sure that the child takes enough on each and every occasion. The problem becomes more acute when the child starts to take solid food and is able to show his likes and dislikes. The mother

may then take refuge in all kinds of manœuvres to "get him to eat", including bribes, threats and distractions Refusal to eat may be exploited by the child as a means of dominating and attracting attention.

Feeding difficulties are often most acute when the child is two or three years old at a time when he begins to show his emerging independence in his desire to feed himself and eat what he wants and not what his mother insists on his having because it is good for him The first step in treating a difficulty of this kind is to allay the mother's anxiety by conducting a careful physical examination to assure her that the child has come to no harm It may be as well also to discover whether the mother has any special reason to fear that the child may not grow up into a vigorous adult, as may be the case if, for example, there is a family history of tuberculosis Otherwise, the doctor should aim at reducing the mother's anxiety, guiding her in allowing the child more freedom in choosing what he will eat and not insisting on his eating too much of what he dislikes.

Most parents know nowadays that thumb-sucking, nail-biting and masturbation are deviations which are of little emotional significance and should be treated with tolerance and without anxiety If, however, such deviations are ··sistent over a long period of time, the child should be referred to a clinic further investigation

Occasional temper tantrums are normal in childhood They may represent ıtbursts of anger against a thwarting parental authority, jealousy towards sibling or, in later childhood, difficulty in adjustment to the tensions engendered by beginning to mix with playmates If the child is usually happy and the parents are otherwise satisfied with his behaviour, nothing needs to be done about the tantrums. They should be regarded as a healthy and natural protest against encroachments, albeit inevitable, on his rights and satisfactions as an individual

Psychoneuroses.—*Anxiety Neuroses* form the bulk of the neuroses seen in practice. The more general principles of treatment have already been dealt with, but there are some special points to be borne in mind in dealing with these conditions. The process of mental *catharsis*, that is to say the discharge of emotion in the presence of the doctor, is especially helpful in anxiety neurosis. Often all that the patient needs is a sympathetic and understanding listener, and if the doctor is able to assure the patient of his interest and does not hasten to interrupt with premature explanations or reassurance, the patient may be relieved of his tension even in a single session At one time it was believed that the anxiety neurosis was an *actual* neurosis, that is to say, that it was due to accumulated tension producing direct physical effects. It was also believed that tension was always due to sexual excitation in the absence of sufficient discharge. This is now regarded as an extreme view, but the doctor should bear in mind the possibility that the patient's symptoms may, at least in part, be due to the practice of coitus interruptus It is certainly true that improvement often occurs when intercourse is accomplished in a more satisfactory fashion, and this is especially so in women when unsatisfactory coitus has been accompanied by anxiety connected with the fear of pregnancy

There is a special form of anxiety neurosis which has been called *traumatic neurosis* and which follows severe trauma While it is seen typically in war, it occurs also after accidents in civil life This neurosis is characterized by attacks of anxiety of the usual kind, broken sleep, terrifying dreams, headache, and irritability, especially towards members of the patient's family. In more

severe cases there is tremor of the head and limbs. There may be amnesia for the actual traumatic incident, especially in the war neurosis. The feature of the trauma which precipitates the neurosis is an apparently inescapable situation threatening the life of the patient. At the time of the trauma there is no way in which the patient can master the situation and the overwhelming anxiety aroused cannot be dissipated by action The repetition of the incident in the waking thoughts and the dreams of the patient may be an attempt to relive the situation and achieve control over it.

Working on a railway line a man had to throw himself down between the rails on the unexpected approach of a freight train. As the train passed over him he saw a broken brake-rod projecting downwards. He felt that death was certain but somehow managed to throw himself outwards between the wheels. He developed a traumatic neurosis.

terrifying dreams in which the incident was repeated and as he walked on the street he had a constant feeling that the buildings were about to fall on him.

When the neurosis persists unrelieved it is usually necessary to go more deeply and to discover, for example, whether the incident was interpreted by the patient as a punishment associated with a previous feeling of guilt. Where there is amnesia or impaired memory for the event the best treatment may be

if he is put into a relaxed state and taken over the events up to the point where the amnesia began. It may be necessary to do this several times before he begins to abreact. The process can be facilitated by making the patient drowsy with an intravenous injection of thiopentone or by giving him light ether anæsthesia. If a narcotic or an anæsthetic is used the incident recalled has to be gone over again when the patient is fully conscious. These methods are not suitable for general practice. During the abreaction the patient may become very excited, shouting and screaming, and may remain in an excited state for some hours afterwards

In traumatic neurosis recovery may be hampered by the existence of a legal action against another party for damages or compensation In some cases the patient is quite conscious of the desirability of maintaining his symptoms so that he will obtain a favourable financial settlement, but perhaps more frequently the persistence of symptoms in such a situation is determined by emotional factors of v ... may be part of ... was rejected by ... r the patient ma ... istice of his cause in the face of an underlying sense of guilt and a conviction of his own culpability. It is necessary to try to deal with these attitudes, but the doctor will often find he is playing a losing game, and that conferences with lawyers and trade-union officials and the pressure of the patient's friends and

relatives will only too readily neutralize the effects of the psychotherapy. The patient should, of course, be told that it is in the interests of his future health to obtain an early settlement of the dispute so that he can then devote himself in a whole-hearted fashion to his rehabilitation

The fact that *hysteria* usually arises out of a personality not readily accessible to psychotherapy renders the prognosis unfavourable for superficial treatment. The patient will often respond to placebos and to the demonstration of attention on the part of the practitioner, but this usually prepares the ground for the fabrication of a new disability. The doctor must be shrewd in dealing with the [illegible]

to adopt the attitude of a firm and rather strict parent who, nevertheless, does not thereby threaten rejection but who remains positive. Hysterical outbursts must certainly be treated in this way, and while superficially the patient may appear to resent the doctor's attitude, it will on a deeper level provide much-needed security and reassurance; it will also help the family and perhaps relieve them to some extent of the guilt aroused by the resentment they at times feel towards the patient.

The *obsessional neurosis* is exceedingly difficult to treat in a radical fashion and the practitioner must not expect striking therapeutic results, he should, however, aim at giving support and reassurance

The patient is always aware of the unreasonable nature of his doubts, compulsions and obsessions, but he is, nevertheless, unable to withstand the impulse to give way to them. He often feels ashamed of his actions and thoughts and may believe that his illness amounts to insanity It is for this reason that he may hesitate to approach the doctor about his symptoms, but his relief is correspondingly great when he finds that his illness is one which is recognized by his doctor. It is in the nature of the complaint that the patient should continually struggle against his compulsions, and it is helpful for him to be assured that it is better not to make these strenuous efforts When the patient is obsessed by the fear of harming someone and has, for example, developed an obsessional phobia of knives so that he feels upset when he sees them and cannot handle them, it is necessary to assure him that he will never give way to the act he fears. Reassurance of this kind may have to be given again and again and it may seem to be quite useless, but in fact it may provide for the patient the necessary support to see him through an acute attack. Obsessional symptoms sometimes accompany a psychosis and the practitioner should always have in mind the possibility of a patient developing an attack of depression When [illegible]

without obvious tension.

[illegible]

Such a patient not only needs her neurosis—she has a right to it. The visit to the doctor may be for her an assertion of her dignity and of her rights as an individual, which should be respected and which it would be cruel to deny her.

Psychosomatic Illness.—It is barely possible to enumerate all the physical symptoms in which emotional factors may and often do play a part. The most obvious and the most frequent is *headache*. In common speech and universal experience the connection between headache and tension, especially frustration, is recognized. Discussion of current emotional problems may be exceedingly effective and should always be considered when symptomatic treatment by analgesics does not quickly bring relief. *Pains and stiffness in the back, neck and shoulders* are worth investigating in the same way before attaching the label rheumatism or fibrositis Such pains are often symptoms of mild depression or of acute resentment, and the truth of this may not be difficult to elicit.

These are the conditions which are probably most readily treated, but spastic constipation with or without the passage of mucus and persistent diarrhœa will

carefully into the patient's routine of work and his periods of rest and recreation; with the support of his doctor he may learn to relax and with firmness he may be induced to delegate work or obtain the holidays he needs. Hobbies and

he left home for a short time to do a job elsewhere (see p. 686). In such a case it may be advisable to draw the obvious conclusion and arrange that the patient should go off on his own and avoid the home situation which upsets him.

Chronic Psychotic Patients.—For every psychotic patient who is in a mental hospital there
of the latter are very
behaviour. There a
live peaceably
hotic patient
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to maintain
the patient at home Fortunately there is usually a great deal of domestic tolerance for such patients, although the family may require the doctor's support and encouragement to maintain their morale in such a long-term task The help of a social worker should be sought in finding suitable employment; if the patient cannot take a job it may be possible with the aid of a hospital Occupational Therapy Department to have him taught some simple pursuit which fashion

Sex turn to their doctors to help them nd it is therefore necessary for

doctors to be well informed in these matters and to be able to act as educators

Some of the most intractable psychotherapeutic problems lie in the field of sexual behaviour. The doctor should, therefore, not expect to be uniformly successful either as an educator or as a therapist Sometimes when it seems

constitutional and physical factors entering into the genesis of symptoms only to the extent which they do in other neuroses They should be treated in the same way, remembering that an inquiry into disturbances in general personal relationships may have relevance to the sexual problem

Competence in the sexual act is apt to be regarded as a measure of virility, and fears of impotence are widespread in our society In early adolescence many boys begin to show anxiety of this kind when they develop the idea that they have an unduly small penis. Arising out of this they may develop feelings of inferiority or shyness, and *masturbation* may be resorted to largely from a need to reassure themselves about the integrity of their sexual functions Guilt about masturbation is reinforced by theories of the harm which it may cause, and the adolescent may come to believe that he has in some way damaged himself so that he will be unable to perform the sexual act as an adult Those occasions when he has to undress in front of others, especially medical examinations, are feared because he believes his sexual inferiority will be noticed and ascribed to his guilty habit. This type of anxiety is so frequent in adolescence that wherever possible the doctor, in conducting a medical examination, should endeavour

be more worried by the nagging idea that his pimples are the result of his masturbation. Masturbation occurs in such a large proportion of males during adolescence with no noticeable effect on sexual performance in marriage that it can be held to be sufficiently proved that it produces no impairment of sexual capacity. This is the kind of reassurance which patients require who are worried about masturbation The doctor may be tempted to feel that fear of the consequences may be a help to the patient in abandoning the habit, but experience suggests the opposite Guilt and self-loathing may drive the patient

observations of animals. Since, however, sexual behaviour in man is affected by the taboos and restraints of the society in which he lives, it is usually necessary for some instruction to be given In most marriages a consistently adequate

performance is not achieved before a year has passed. The patient who complains of an inadequate performance should be reassured and advised to give up his strenuous attempts and his intense preoccupation with his failures in the assurance that, as many other men have discovered, his difficulties will disappear with time.

[illegible]

almost universally recognized that satisfaction for the woman is a reasonable aspiration in the marital relationship. As yet, however, and in spite of this knowledge, a considerable proportion of women are unable to achieve any marked degree of satisfaction. It is possible, indeed, that some women are [illegible]

tionistic and to explain that this is a common and quite healthy response to [illegible]

[illegible] Associated [illegible]

remember, too, that guilt over masturbation, and a belief that incapacity in the sexual act may thus have been caused, may require to be discussed with women patients.

[illegible]

faction. *It is often assumed that the natural duration of coitus tends to be* shorter in the male than in the female. While there is no real evidence to support [illegible]

and in different individuals. The way in which sexual satisfaction is achieved is dependent on factors in the upbringing similar to those which determine the personality. Domination and submissiveness, aggressiveness and tenderness, the pleasure derived from stimulation of extragenital as compared with genital areas, all these are components which may vary from one person to another. The *fact* that their sexual behaviour may seem to deviate from an imaginary norm is a cause of concern to many patients It should be pointed out that there is no normal or standard pattern and that behaviour is perverse only when it is persisted in despite the protests of the marital partner, or when instead of being a preliminary to the normal completion of the act it takes precedence over and is a substitute for it. If there is *perversion* defined in this way, the patient requires psychotherapy which is probably beyond the resources of the practitioner.

From what we know of human sexual behaviour it would appear that we

are all bi-sexual to some extent. In a very high proportion of both men and women we can find some evidence in the life-history of at least transitory attachments to members of the same sex, and in many cases there has also been some overt expression of homosexual activity. It is very important therefore not to over-estimate the prognostic significance of a homosexual episode in a life-history, a good marital adjustment can occur even when there has been a quite persistent pattern of homosexual activity, provided, of course, that the individual concerned has sufficient heterosexual feeling to make such an adjustment possible. The practitioner's own prejudices may create a barrier to the full investigation and understanding of these patients; he should therefore try to be as objective as possible In assessing the depth and significance of a homosexual relationship the factor of privation has to be taken into account. When men live isolated from women, as, for example, in the fighting services, it is well known that homosexuality is more liable to occur It should also be remembered that neurotic factors may isolate an individual from the opposite sex, a feeling of inferiority because of a deformity, a speech defect or a chronic skin lesion, may reduce the individual's capacity to meet the opposite sex and lead to homosexual behaviour as a substitute outlet Cases of this kind provide the practitioner with considerable scope for treatment. He may encourage the patient to take up social activities by carefully graduated stages, while the energetic treatment of any handicapping condition may give the patient more hope and confidence and the doctor's positive attitude and reassurance may help his self-esteem

ALCOHOLISM AND DRUG ADDICTION

It is difficult to define precisely what should be included under the term " drug addiction ". Addiction may be said to exist when a state of dependence has clearly become established. This condition of dependence is seen when the use of the drug is discontinued the addict then develops *abstinence symptoms* characterized by various constitutional disturbances and the phenomenon called *craving*. If these criteria are applied to the use of alcohol and tobacco, it is obvious that most people who drink or smoke are not addicts, on the other hand it cannot be denied that there are many alcoholics and also heavy smokers who are undoubtedly addicts

As already pointed out, with most drugs of addiction there are two types of dependence which have to be clearly distinguished :

Treatment has to be directed therefore in the first place to diminishing or abolishing the physical dependence on the drug, but when this phase is over and complete withdrawal has been effected the much more difficult problem of handling the craving remains, and this requires psychotherapy of some kind.

Treatment which stops at physical measures can only lead to relapse. Nor should it be assumed that when one euphoriant drug is replaced by another any degree of success has been achieved; the patient is still, and perhaps more deeply, in the clutches of his craving while a new addiction in the form of a new pathway to his desired euphoria has been provided for him. Obvious examples of this error in treatment can be provided from the past. As is well known, Freud was enthusiastic for a time about the virtues of cocaine as a cure for morphinism: it is possible to repeat this error today by using a new drug pronounced safe by its manufacturers before its true character has become known. Up to the present no such safe substitute has emerged and all such claims should be viewed with suspicion.

The euphoriant character of some barbiturates, especially perhaps the short-acting type, permits a true addiction to these drugs which, in numbers, is probably the most formidable problem of addiction, apart from alcohol, in those countries where the control of drugs is otherwise strict. Amphetamine, used as a substitute for replacing alcohol or drugs, can lead to a similar state of affairs.

ALCOHOLISM

Various stages in the development of alcoholism can be distinguished which require different kinds of treatment.

Early Alcoholism.—Propaganda in recent years is leading to a changed attitude, and as a result, drinkers who are beginning to find that their drinking has become a problem to them are more readily turning to their practitioners for help. At this stage, psychotherapy of a supportive type can succeed, aimed at reinforcing the motivation of the alcoholic to stop drinking. The attitude of the doctor should be the same as is described in dealing with neurotic problems although only a minority of alcoholic patients show any signs of neurosis. It should be explained to the patient, even at this stage, that no amount of drinking is possible for him without relapsing. It is at this stage that patients who are genuinely anxious to be helped can be tried on disulfiram (tetraethylthiuram disulphide; its original and most common proprietary name is Antabuse). This drug, when taken over a period, results in an unpleasant reaction in the patient when alcohol is subsequently consumed. Its use should be avoided in patients who show obvious abnormalities of personality or who have reached the reckless, self-destructive stage of alcoholism; in such cases its administration constitutes a real danger. The drug should also be avoided in patients suffering from hepatic or circulatory disorders and in diabetics who are not adequately controlled by diet and insulin. When the patient has to receive a general anæsthetic, the drug should be stopped for some days previously.

Treatment begins with the oral administration of two 0·5 g. tablets on the evening of the first day and one tablet on each of the following five to six days. Thereafter a maintenance dose of half a tablet (0·25 g.) can be given every day, and in some cases even this dose can be reduced to 0·25 g. every other day. At the end of the first week's treatment it is usual to administer alcohol to demonstrate to the patient that he c [illegible] small quantity and that the effects are not only ver [illegible] dose, e.g. 3 teaspoonfuls of whisky [illegible] and the patient should be kept under observation for two or three hours afterwards lest there should be a delayed reaction. The symptoms which normally

that this reaction will develop whenever he takes alcohol and that if he takes a large quantity it is likely to be much more serious and might be very dangerous He should also be warned not to take paraldehyde, which has the same effect as alcohol, paraldehyde being the hypnotic preferred by many alcoholics. Severe reactions can occur even with a test dose and, for this reason, the test should be carried out in circumstances in which the doctor is prepared to deal with them by the use of oxygen inhalations and respiratory stimulants such as nikethamide, 5 ml. of a 25 per cent solution intravenously Provided the patient avoids the risks which have been mentioned, there are seldom any obvious side-effects from the use of disulfiram, but a few patients complain of tiredness and diminished sexual potency

It is obvious that this treatment is not likely to succeed with an unwilling patient, and even with a willing patient it should be regarded only as ancillary to the main form of treatment, which is psychotherapeutic

few places elsewhere and has done more in a few years to reclaim alcoholics than has ever been done by purely medical endeavour As a rule, however, medical treatment must precede successful rehabilitation by A A

a suitable nursing home or hospital has become necessary. He should be informed that a period of some months may be required to effect recovery and that thereafter further efforts on his part and usually the help of A A will be required to keep him well.

In the later phases of alcoholism deteriorating mental illness can result, e g Korsakov's psychosis. The problem is then one of permanently impaired capacity requiring psychiatric care More important in ordinary practice is *delirium tremens* In this condition treatment should have three aims :

Sedation.—The drug of choice is paraldehyde in generous doses—8 to 16 ml (2 to 4 fl dr) by mouth or 8 to 12 ml (2 to 3 fl dr) by intramuscular injection. Barbiturates are best avoided because they cause euphoria in the young and confusion in the old In some cases, where restlessness and excitement are intense, the patient may be greatly helped by giving electro-convulsive therapy.

The Correction of Vitamin and Hormonal Deficiency.—During the acute

tinues). Thereafter a reduced dosage by mouth or injection should be given once daily for a further week (ascorbic acid 0 5 g, aneurine hydrochloride 0·25 g, nicotinamide 0·16 g, pyridoxine 50 mg.). Corticotrophin, 25 mg. six-hourly, will reduce delirium and excitement within a few hours and shorten the course of the illness.

A careful watch should be kept on the condition of the chest and antibiotic treatment introduced if there is reason to suspect the onset of pneumonia.

DRUG ADDICTION

In some countries there are few addicts to the scheduled drugs of addiction (e.g. morphine derivatives, pethidine, cannabis indica and cocaine) and in these circumstances physicians will regard their therapeutic task as being mainly *prophylactic.*

Since non-habit forming local anæsthetics are available as substitutes for cocaine (except perhaps for direct application to the eyes, ears, nose and throat), no problem of creating addiction to cocaine need ever arise. In the case of opiates, however, care has to be exercised. It should be remembered that no person is immune to opiate addiction Prolonged administration will be followed by abstinence symptoms in everyone, and this stage can be reached in the case of diamorphine after only 10 to 12 injections. For this reason the risk of addiction should always be kept in mind although the physician should not be so cautious as to avoid the use of opiates when they are clearly indicated.

special importance when repeated doses have to be given. Especially in post-operative treatment, preference should be given to the use of suppositories rather

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under strict supervision as soon as possible so that the withdrawal of the drug can be carried out. Withdrawal symptoms always occur and call for careful management. Insomnia, restlessness, anorexia, excessive perspiration and

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from a repetition of the treatment, nothing has been gained. Nowadays *rapid withdrawal* over a period of two weeks is most in favour. The dosage on which

the patient stabilizes without developing abstinence symptoms should first be ascertained This is likely to be less than the dosage which the patient declares he has been getting; he is naturally anxious to postpone the effects of withdrawal ... ascertained the dose should be reduced by one-

of expectation can be reduced. ...

... barbitone 1 3 g (20 gr.) daily, can be given,

also be reduced very effectively by frequ...

... formal psychotherapy to the morphine addict is a formidable and ... come to respect the firmness ... with him afforded ... mal psychotherapy takes place.

The Treatment of Cocainism is along the same lines, but the withdrawal ... are trivial compared to those of the morphine addict and are not ... justifiable to give a cocaine addict ... iptoms ... **tion.**—In the case of the marihuana ... ular, the addiction is best regarded ... pander

T F. Rodger

DISEASES OF THE NERVOUS SYSTEM

INTRODUCTION

TREATMENT of organic nervous disease is a double challenge; the one to the resource of the physician and the other to the conscience of the community. The doctor's problem goes far beyond mere administration of drugs: he may have to rely on physical and educational forms of therapy, and he must often depute active treatment to others. The problem for the community is an obligation to provide for those who need constant care and to find employment for those who can work, no matter how limited their capacity

Treatment begins with the doctor's first question to the patient, before any attempt at diagnosis. Careful history taking and thorough examination are essential preliminaries to treatment. they establish mutual confidence and understanding as a foundation upon which to build effective and rational therapy. A diagnosis having been made, the appropriate pill, powder or potion is prescribed, in accordance with the physician's knowledge and experience of the condition The actual medicine may be specific or symptomatic in its action; it may cure some reversible process in the nervous system, or merely relieve distress arising from an intractable cause Such treatment, however, is almost automatic and scarcely touches the human problem in nervous disease. The need for wise psychological handling is not exceeded in any other branch of medicine. Bizarre ideas of the function and form of the nervous system give rise to fantastic fears whenever there is a threat to its integrity. Such fears breed *symptoms of no organic significance and yet may constitute the main problem in* treatment Strenuous efforts in several directions are needed to dispel fear and [illegible]

offered to the patient, they remain a mystery to him, and anxiety is the child of mystery

Discretion and judgment must colour pronouncements. The whole truth cannot be revealed to many patients, they must have, nevertheless, a statement which satisfies their reason, or be assured that the physician understands and is neither alarmed nor surprised by the course of events. There is no standard pattern for the explanation, how much or how little is told depends on the nature of the disease, the intelligence of the patient and the personality of the doctor The use of technical terms and the naming of a definite diagnosis in progressive disease with an unfavourable prognosis should be avoided On the other hand, it is often expedient to define and delimit a nervous lesion to an intelligent patient by giving the whole explanation of a static or regressive condition Thus apprehension can be cut short and adaptation encouraged Natural adaptation is characteristic of the resilience of the patient and may go a long way to the achievement of a satisfactory final result Most people, however, require help and guidance They must be told how much activity can be reason-

ably expected of them in the face of disability and without prejudice to health. When the invalid is capable of employment it should be the pleasure and not the task of the physician to give particulars of the industrial potential of the patient to employer, social worker or resettlement officer. The whole problem of the social welfare of the disabled—their rehabilitation, training and employment—is fully discussed on p 838.

Little has been said about the more acute forms of nervous disorder. These will be considered under appropriate headings because generalizations are scarcely possible. An attempt has been made to lay down certain broad principles for the care and treatment of the great majority of those afflicted with nervous disorders.

INFECTIONS

Infective processes involving the nervous system have to be considered from several points of view Chemotherapeutic agents and antibiotics are used in combating general infection so that the invader succumbs to the therapeutic assault. In treatment of infections of the nervous system, the same techniques are applied The course to be followed in dealing with meningitis in its various forms has been fully discussed elsewhere (see pp 30, 57, 132).

It is important to prevent the spread of infection to the nervous system from an adjacent or remote source Adjacent foci may require surgical care, and indeed whenever abscess formation occurs, the general principle is to deal with the condition surgically Loculations of pus anywhere are a potential source of danger no matter how well encapsulated they may be for a time There is, however, no hard and fast rule, clinical judgment only can determine the circumstances indicating a therapeutic assault or a masterly inactivity One can merely point out that immunology may yet offer a far more ideal solution to the problems of infection of the nervous system, the appearance of so many powerful therapeutic agents has in no way altered the basic fact that the body marshals forces to kill off an invader These words reiterate a warning against the uncritical use of antibiotics If, however, clinical judgment discerns a threat to the nervous system through infection, the use of drugs given to combat infection should be wholehearted and complete.

LATE EFFECTS OF MENINGEAL INFECTIONS

Depending on the age of the patient, organized adhesions in the basal regions of the brain and in the posterior fossa may produce varied hydrocephalic effects In infancy, before the cranial sutures have firmly fused, the result differs from that produced by comparable lesions in later life. The younger the patient, the greater is the characteristic ballooning of the skull above the level of the eyes and ears and the smaller the absolute increase in intracranial pressure. If the sutures have not united, gradual expansion of skull volume may occur with little or no impairment of intellect and cranial nerve function. Increase of intracranial pressure may cause incompletely united sutures to separate and compensate slightly for the increase. If the cranial vault is unyielding, the rise in pressure soon interferes with the level of consciousness, coning may occur and constitute a serious surgical emergency. When hydrocephalus expands the ventricular system, spontaneous cure may sometimes follow rupture of the lamina terminalis, since drainage into the subarachnoid space may restore

hydrostatic equilibrium. Careful measurements of the cranial dimensions should be recorded monthly in the case of the hydrocephalic child. The neuro-surgeon's advice should be sought in all these cases, because he may be able to re-establish the cerebrospinal fluid circulation by the operation of third ventriculostomy, or by draining the lateral ventricles into the cisterna magna (Torkildsen's operation) One word of warning should be given; when the brain is expanded and the cortex is a mere shell, sudden collapse of the ventricular system may tear the small veins which traverse the subarachnoid space from the brain to the superior longitudinal sinus, with the formation of sub-dural hæmatoma.

The [illegible] nction [illegible] some [illegible] very necessary requirement for co-operation in treatment. Owing to prolonged pressure on and thinning out of the infundibular region of the third ventricle, endocrine imbalance may follow. Thus some hydrocephalics become giants and some dwarfs. The writer does not know of any useful or rational treatment of these complications.

Apart from hydrocephalus there are two causes of severe residual disability following meningitis—destruction of cerebral tissue by the toxic impact of the acute illness and ischæmic change from obliteration of the blood supply by progressive cicatrization of organized exudate. Clinically these two processes are difficult to distinguish, but there is no radical relief from either. In meningitis both these causes may contribute to a break in the physiological integrity of the cerebral crura or even of the spinal cord.

In the former, the patient lies in a state of decerebrate rigidity, more often [illegible] verse section of the cord with consequent paraplegia (*q.v.*) More discrete focal residual disability may occur from cortical lesions and must be treated as described under the appropriate sections dealing with hemiplegia, paraplegia, epilepsy, dysphasia and mental defect Unfortunately cranial nerve function may be grossly impaired. Of all the cranial nerves to be irreversibly and completely damaged, the auditory nerve is most frequently affected. Quite apart from the possible role of infection, a specific toxic effect may be exerted on the auditory nerves by streptomycin when this drug is used. Amaurosis is an unusual sequel but is often accompanied by mental impairment which deprives the blind of the many advantages in training described in the following section Paralytic strabismus is not uncommon as a permanent residual defect. Often much can be done for the patient with permanent diplopia and it is always worthwhile consulting an ophthalmologist with a view to considering corrective operative measures on the extrinsic ocular musculature.

SUPPURATIVE ENCEPHALITIS

Treatment of brain abscess depends on the ætiology of the condition. Pus formation within the brain may be due to venous thrombotic spread from an adjacent nidus of infection in the accessory air sinuses of the skull, or indeed from infection of any of the integuments of the brain. Infective processes at a distance, particularly in the lung and endocardium, may provide the origin for

metastatic spread to the brain. Adjacent infections have to be dealt with by antibiotic therapy and more often than not by surgical intervention Treatment directed towards the source of metastatic infection makes its own special demands. It should be remembered that abscess of the brain from bronchiectasis is no longer the fatal condition of the days when antibiotics were not available. Drainage and excision of a brain abscess is a neuro-surgical task and does not concern us here No brain abscess, however it may be treated, leaves the brain unscathed. Therefore the medical problem is the treatment of the residual effects. In the acute phase of the illness as well as later, epilepsy—the most frequent complication—often occurs One should, therefore, protect the individual from convulsive episodes through the pre-operative, operative and post-operative phases by adequate exhibition of appropriate anticonvulsant drugs Dysphasia, mental defect, personality change, as well as hemiplegia and ataxia—sensory or cerebellar—present their own peculiar problems and are dealt with elsewhere in this section

Other infections of the nervous system are viral invasion of the brain and meninges, and protozoal infections. Treatment of such conditions is purely symptomatic in the former group but may be specific in the latter. For the purpose of exposition of the problems which confront the physician in dealing with such illness one can scarcely give a detailed account of procedure on an ætiological basis Thus, one has to adopt the rather untidy method of dealing with treatment according to symptomatology and the anatomical site of the lesion

HYPERTHERMIA

Infections may be general and disturb the visceral functions of the nervous system as part of a general toxæmia, or those visceral functions may be disordered by infection primarily within the central nervous system. Some specific fevers manifest themselves by such a rise in body temperature that by its severity it may cause ultimate irreversible damage to the thermostatic functions of the brain. This also applies to primary disease of the brain whether infective, traumatic, vascular or neoplastic. Hyperthermia is always a threat to life and should be controlled in time A few elementary points are germane to understanding the basic problem of hyperthermia. The patient may be pallid, his skin cold and dry yet his blood temperature may be above 107° F. This high temperature is an expression of the failure of the body to lose heat by radiation and evaporation In the periphery the skin vessels are tightly constricted and the sweat glands have ceased to act. Rational treatment must, therefore, attempt to bring about peripheral vascular dilation and sweating or its equivalent Artificially produced vascular dilation in the periphery can be achieved by mechanical means The patient should be stripped of his clothing and bed-clothes His skin should be subjected to rough friction until it is red Sweating does not follow, but the erythematous skin should be kept wet by spraying or washing continuously with cold water, and a continuous stream of air from electric fans should be directed on to the body surface. In addition, ice may be applied to the reddened skin. Only when the temperature fails to come down with these measures should recourse be made to stomach or rectal lavage with ice-cold water The indications for starting these vigorous measures depend on the rapidity of rise of temperature as well as the absolute level of the rectal temperature When this has been lowered to a leve

of 102° F., cooling treatment should stop, but the rectal temperature must be taken hourly during the unstable few days which necessarily follow the breakdown of such a fundamental biological mechanism as thermostatic control.

Disorders of Water and Electrolyte Balance

It must not be forgotten that acute infections of the nervous system and chronic nervous states with impaired consciousness are complicated by dehydration and electrolyte loss. The picture of gross interference with neural function should not obscure this aspect of disordered metabolism. Lack of attention to the problem of water and electrolyte balance may create a vicious circle; the coma of primary disease of the brain may be obscured by the altered state of the body milieu with central nervous repercussions (see p. 96).

EXTRAPYRAMIDAL DISORDERS

As the chronic results of virus encephalitis are mainly concerned with disorders of extrapyramidal function, the entire group of such disorders, irrespective of ætiology, will be considered as a whole

Parkinsonism.—This syndrome is characterized by muscular hypertonia and hypokinesia The striated muscles are rigid in contrast with pyramidal spasticity and there is the utmost economy of voluntary movement independent of the agitation of tremor Drugs which relax muscle are therefore indicated, and activity designed to widen the range of joint movement is to be encouraged both by direction of the daily routine of life and by physiotherapy. In severe cases the greatest burden imposed by the disease is the fixity of posture. Thus the grossly disabled person has to be turned in bed, helped out of a chair and looked after as he walks, because rigidity of muscles has so interfered with

... al treatment (see p. 822)

ment and may be prescribed in doses of the tincture increasing from 1 3 ml. to 4 0 ml. (20 to 60 min.) thrice daily unless the limit of tolerance is reached before the suggested maximum dose is given The patient usually adapts himself to massive dosage, but agitation, confusion and vomiting are indications for reducing the amount of stramonium given

some, atropine may be added in the form of the tincture of belladonna, 0 3 to 0 9 ml. (5 to 15 min) thrice daily. Drugs prescribed to reduce salivation necessarily paralyse accommodation. This unpleasant side-effect can be ... drop of a ½ per cent. aqueous solution of eserine

... lrugs ... particular advantage over the original di... ne hydro... l), which combines a

Useful activity should be encouraged and both physiotherapy and occupa-

to a point necessitating institutional care. The very nature of the condition may project something of its hopelessness to the doctor's attitude, to which the patient is by no means insensitive Sufferers from Parkinsonism benefit from *the enthusiasm and diligence of the physician.*

A distinction must be made between treatment of post-encephalitic Parkinsonism and that of senile Parkinsonism In the former, visceral disorders are more frequent than in the latter, therefore, the atropine-like drugs should be used in preference to the antihistamine preparations. The senile cases have often a degree of dementia which takes away the element of co-operation so necessary in achieving the best result Generally speaking, massive therapy is better tolerated and more widely indicated in the post-encephalitic type of case than in the senile.

Narcolepsy.—This condition, sometimes a sequel of encephalitis, has to be carefully distinguished from hypersomnia Narcolepsy is paroxysmal and sleep may overtake the patient in spite of all efforts to remain awake Unless the condition is adequately controlled by appropriate treatment, the limitations imposed on the patient are comparable to those of epilepsy There is, however, no real connection between epilepsy and narcolepsy There is an association between paroxysmal overwhelming sleep and cataplexy—a disorder which, without loss of consciousness, causes the patient to fall into a state of muscular atonia when-

tions in capsule form (spansules) to give longer absorption time: thus the initial dose may be larger and the taking of tablets at inconvenient times obviated. With such a disturbance of normal sleep rhythm it is not surprising that insomnia overnight is often troublesome This can be countered by a suitable hypnotic dose of a short-acting barbiturate such as pentobarbitone sodium (Nembutal), 45 to 90 mg (¾ gr to 1½ gr.). Amphetamine should never be prescribed without due consideration of the risk of addiction This risk is not so widely realized as it should be, the drug should not be allowed to fall

isolation and the administration of certain drugs reputed to have a specific effect. The child should be nursed in bed for a month, away from noise and

bustle He should receive no visitors and should not read or listen to the radio. Acetylsalicylic acid can be administered in 0 6 to 1 g. (10 to 15 gr.) doses, thrice daily, in the form of aspirin or calcium aspirin. Such a dose is well tolerated by a child of twelve years.

Excessive movement requires the protection of a padded cot-bed. Violent and continuous movement may break the surface of the skin, especially over the bony points. Friction can be reduced by suitable padding fixed in position by adhesive strapping.

To give the patient rest, chloral and barbiturate may be successfully combined as follows ·

℞	Chloral Hydrate	0 6 g. (10 gr.)
	Sodium Phenobarbitone	30 mg. (½ gr.)
	Syrup of Orange	2 ml. (30 min)
	Water	to 15 ml. (½ fl. oz.)

The mixture may be given two to four times within twenty-four hours, according to the severity of the condition In more violent chorea, sedatives have to be injected Sodium phenobarbitone in 0 2 g. (3 gr) doses may be

sating for the fluid loss of sweating. In severe cases care must be taken to see that the chloride loss from sweating is balanced by adequate salt in the diet.

The patient must be watched after treatment has abolished abnormal movement. He is potentially a sufferer from other manifestations of rheumatism and accordingly requires treatment and observation, though it is true that rheumatic carditis is a much less common sequel to chorea than to rheumatic fever

Chorea insaniens and chorea gravidarum are merely variants of rheumatic chorea and demand the same general treatment. The violence and mental aberration accompanying these disorders may demand much heavier sedation than that indicated above

COMPLETE AND PARTIAL TRANSVERSE LESIONS OF THE SPINAL CORD

Initial treatment depends on ætiology. Thus traumatic and infective lesions of the spinal vertebræ call for the urgent co-operation of orthopædic and neurological surgeons Usually some means of fixation is essential but can be left to the technical resource of the specialist. Extramedullary and intramedullary tumours must be investigated by myelography to determine the feasibility of operation. For the physician, treatment of the paraplegic resolves itself into several activities Bedsores ought to be prevented rather than treated. In any illness necessitating prolonged rest in bed, bedsores constitute a threat which is intensified when the trophic functions of the tissues are disturbed by organic disease of the nervous system Added dangers are encountered in certain lesions of the spinal cord when flexor spasms cause friction, and incontinence of urine and fæces macerates and infects the skin. Care of the skin involves avoidance of prolonged pressure on any limited area, keeping the surface as clean as possible and attempting to toughen the tissue by various means The first is achieved by moving the patient at least every two hours. The skin over

the heels, the malleoli, the sacrum and anterior superior iliac spines may have to be protected by padded rings. The patient should lie on a sorbo-rubber mattress which is easily cleaned, is comfortable to lie on and dispenses with such anachronisms as water or air beds. Fæcal contamination of the skin is unavoidable when sphincter control is lost, but the fouled area should be cleaned frequently. Ulcerated areas, if frankly infected, may be treated by application of a combination of topical antibiotics in a suitable base, such as neomycin, 2 5 mg, and gramicidin 0 25 mg. per gramme of ointment (Graneodin). Washing with Eusol when the bedsore is being dressed is useful in aiding separation of sloughed tissue. Recently silicone barrier creams have been applied to the skin threatened with ulceration and to areas surrounding actual bedsores. This method of treatment holds out some prospect of keeping the skin waterproof and protecting it from infection

Care of the bladder in paraplegia has two aspects—control of infection and avoidance of back pressure on the urinary tract The former may be dealt with by suitable systemic chemotherapy or the exhibition of a suitable antibiotic. The latter involves regular emptying of the bladder by methods which largely depend on the exigencies of the particular case If the lesion is above an intact lumbo-sacral cord, there is prospect of the development of an automatic bladder. Automatic emptying of the bladder does not occur immediately after an acute lesion Urine accumulates and overflow incontinence develops unless the distended bladder is emptied by manual compression applied through the anterior abdominal wall or by catheterization To encourage the early development of automatic activity, a self-retaining catheter of the Foley type is introduced, a clip is put on the catheter and is released every four hours. If the bladder retains a considerable quantity of residual urine when the clip is released, the administration of carbachol may be considered, the test dose of ½ ml. is injected subcutaneously and, in the absence of any cardiovascular collapse, the drug may then be given in doses of 2 ml as required The older method of tidal drainage certainly encouraged the development of automatic emptying of the bladder, but its main use was to prevent urinary infection by irrigation with a weak antiseptic. This practice has been almost entirely replaced by the use of the self-retaining catheter under antibiotic cover. When the bladder is foul and the [illegible]

tactile and [illegible] and thermal [illegible]

but it may be necessary to give guidance regarding suitable work and positive dangers. Syringomyelia is probably neoplastic in nature and X-ray therapy is often employed in its treatment. This may delay the rate of progress of the [illegible]

may have developed and decalcification of bone may be followed by pathological fractures from minimal trauma such as turning the patient in bed. In these desperate cases the patient is often so much under the influence of drugs

If anything surgical has to be undertaken, it should be done quickly. Papilloedema is a sign of grave urgency. Delay in submitting the case to a neuro-surgeon prejudices sight, muscular power, co-ordination and even life itself. Too often a patient with papilloedema resulting from a cerebral tumour syndrome is subjected to a lumbar puncture in spite of full clinical awareness on the part of the physician. Sometimes this procedure is fatal to the patient. If no papilloedema has developed, lumbar puncture is comparatively safe. The clinical indications of increased intracranial tension are usually clear enough to render lumbar puncture quite unnecessary. Rapid deterioration into coma a few hours after lumbar puncture has been carried out is a frequent sequel. With relief of pressure in the subarachnoid space the tumour expands, becomes oedematous and displaces the base of the brain downwards so that either a medullary or tentorial cone develops. Only prompt action by the neuro-surgeon in tapping a ventricle can avert disaster. The process of coning may occur

the ventricle.

Successful removal of the tumour may enable the patient to return to his work, and indeed to work more efficiently than for months previously. Residual dysphasia of moderate degree will respond to the care of the speech therapist. Hemiplegia or paraplegia may indicate the need for vocational training or special employment. If epilepsy is a symptom of tumour, its removal may not abolish seizures. Usually the epilepsy can be controlled by adequate anticonvulsant treatment. The patient should have a maintenance dose of phenobarbitone over the whole period of convalescence, and, after recovery, for a period of at least two years.

TRAUMATIC DISEASE

Generally speaking, the treatment of traumatic lesions is the concern of the surgeon. After surgical treatment or when no surgery has been necessary, residual symptoms become the province of the physician. At no time has the importance of clear thinking about head injuries been greater than at present. The risks in industry ar

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attitudes to the general problem of head injuries, with the result that many a

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litigation is to be deplored. Post-concussional symptoms of any severity and duration are unlikely to improve pending the process of legal proof. Nor is it

advisable to attempt psychotherapy until final settlement is made, for there is every reason for the patient to remain ill. A sense of grievance engenders self-pity, which is followed by the development of a post-traumatic neurosis, the magnitude of which must match the magnitude of the sum claimed. Every effort must be made for a true assessment as soon as possible, and not the least important part of treatment is to expedite ultimate settlement in so far as the physician is able to do so.

The term concussion is an arbitrary one and is best restricted to signify brief loss of consciousness immediately following a head injury. No one will put a time limit to the duration of loss of consciousness in defining the term concussion, and it is therefore difficult to mark the point in time beyond which continued loss of consciousness denotes cerebral contusion Presumably the post-concussional state must of necessity be a sequel to loss of consciousness from head injury It is surprising, however, to note the wealth of symptoms which may occur after a head injury not accompanied by loss of consciousness the symptoms of which bear a strong resemblance to the generally accepted description of the post-concussional state No doctor can be in a position to help such cases unless he appreciates this point of view. Light-headedness, giddiness on stooping or alteration of posture, intolerance of heights and headache can scarcely be abolished by the most emphatic reassurance by the doctor to his patient that these symptoms are of no morbid significance

Apart from the common picture of the post-concussional state, other residua may follow head injury either as immediate, later or remote manifestations. The most immediate threat, apart from the effects of contusion, is extra-dural hæmorrhage from tearing of the middle meningeal artery. This constitues a [illegible]

development of the symptoms and signs of sub-dural hæmatoma from rupture of veins which traverse the subarachnoid space. Treatment of this condition is entirely dependent on accuracy of diagnosis Too often sub-dural hæmatoma is wrongly diagnosed as cerebral thrombosis, uræmia or diabetic ketosis. Coma is present in all these conditions, but sub-dural hæmatoma may cause palsy in common with cerebral thrombosis while albuminuria occurs with uræmia and glycosuria with diabetes If the possibility of sub-dural hæmatoma is not [illegible]

liable to occur in the aged, in the arteriosclerotic and in cases of cerebral atrophy from whatever cause The insidious march of symptoms such as headache, personality change, disorientation, dilatation of the pupil on the side of the hæmatoma, contra-lateral hemiparesis and later decerebrate rigidity are indications for exploration by trephining. Fluctuation in the mental state, variations in the depth of coma and the fact of a head injury two or three months previously suggest the possiblity of sub-dural hæmatoma when a clinical picture is present with any combination of the signs and symptoms described. The later and permanent sequels of head injury—dementia, aphasia and epilepsy—are considered elsewhere. It is good practice in cases of head injury to give a maintenance dose of phenobarbitone in sufficient amount to avoid convulsions

VASCULAR DISEASES OF THE BRAIN

Congenital Aneurysms with Subarachnoid Hæmorrhage.—Some consideration must be given to the problem of handling a fresh case of subarachnoid hæmorrhage. Frequently coma, with signs of meningeal irritation, confront the doctor, who may have had no previous experience or knowledge of the patient. Once the diagnosis has been made, it must be decided whether the patient should be treated at home or removed to hospital The risk that transport and change of posture may precipitate further bleeding must be weighed against the advantages of constant observation and skilled nursing.

The clinical picture of subarachnoid hæmorrhage from aneurysms varies [illegible]

ment and, later, avoidance of exertion and emotional tension. The majority of *patients recover with such care, but when deepening coma follows from increasing* cerebral compression a fatal termination is almost a foregone conclusion, which cannot be avoided by repetitive lumbar puncture in the hope of relieving the pressure Recently the technique of combining induced hypothermia with chlorpromazine (Largactil) has been used to control hæmorrhage and to reduce the metabolic requirements of an ischæmic brain. This technique is said to postpone the hazards of operation and to enhance the chances of a satisfactory [illegible]

[illegible] tion by angiography is easier because it can then be carried out on the appropriate side. If there is no focal evidence, angiography may have to be repeated on each side. Naturally angiography must wait until signs of meningeal irritation have disappeared. Between the events of hæmorrhage and angiography it is ideal to have the patient hospitalized because of the danger of daily activity precipitating [illegible]

aneurysm in the course of the middle cerebral artery. When direct attack by *exposure and ligation proves impracticable,* ligation of the internal carotid may be advised

Naturally hæmorrhage may prejudice the functions of the brain as a whole, but such cases are unlikely to result in permanent dementia. Ischæmia beyond the site of the aneurysm may leave evidence of permanent impairment of hemisphere function and the problem becomes that of residual hemiplegia or dys- [illegible]

eye, or sensory impairment over the face Ophthalmoplegia, when permanent, requires the help of the ophthalmic surgeon, who attempts to compensate for palsies by operations for the recession or advancement of tendons of the extrinsic

ocular musculature. Analgesia in the face may require special precautions when the corneal reflex is abolished.

Arterio-Venous Aneurysm.—When free communication exists between the internal carotid artery and the cavernous sinus, pulsating exophthalmos on the side of the lesion is evident. The condition should be treated surgically as soon as is practicable after the injury—the usual precipitating cause. Ligation of the carotid artery on the side of the lesion is the usual treatment. The operation is carried out after the patient has been conditioned to occlusion of the circulation by compressing the artery for increasing periods of time.

Cerebral Hæmorrhage, Thrombosis and Embolism.—Acute vascular accidents disturbing the functions of the brain are of dramatic onset. Although this is not the place to give detailed consideration of differential diagnosis, some attention must be paid to ætiology because no treatment can otherwise be rational. By far the greatest number of vascular catastrophes in the brain occur after the fifth decade, and consequently the presence of degenerative change in this group must be assumed. Usually vascular changes are general and evident in situations other than the brain. Hypertension is the usual common factor. Thus, prevention of a certain number of vascular accidents must depend upon the treatment of the hypertensive state (see p. 584). Sudden manifestations of vascular disturbance are due to rupture of an aneurysm, already considered, embolism, thrombosis or hæmorrhage.

Cerebral Hæmorrhage.—This is a comparatively infrequent occurrence. Indeed, it is doubtful if true hæmorrhage from primary rupture of a blood vessel occurs except in the case of aneurysm, either congenital or mycotic, acute encephalitis, necrotic neoplasia and polyarteritis nodosa. If rupture of arterial vessels in the brain occurs, it is difficult to see how bleeding can be arrested. Blood is released into the intercellular spaces of the organ at a head pressure approaching that of the systolic blood pressure. Thus, arterial hæmorrhage in the brain is almost necessarily fatal, whereas hæmorrhages from capillaries and venules may damage the brain but do not necessarily kill the patient. Treatment of cerebral hæmorrhage must be expectant and symptomatic. The care of the patient is that demanded in the treatment of coma. Such complications as hyperpyrexia and pneumonia are considered elsewhere.

Cerebral Thrombosis.—It is important to recognize that prodromal symptoms of cerebral thrombosis exist. Focal disturbances of brain function such as transitory paresis, varying in duration from a few minutes to a few hours, may indicate spasm in an arterial twig. When complete recovery from such an episode ensues, it is assumed that the process is reversible; ischæmia has produced prolonged suspension of function, short of that due to irreversible change. In these circumstances it may be assumed that no thrombosis has actually occurred apart from that which may or may not have taken place in a silent area of the brain. Irregularities in the lumen of vessels, sometimes with the addition of spasm, may produce mural thrombi within the vessels. Thus the way is paved for the final thrombotic event with complete occlusion and ischæmia beyond the point of closure. Before the final event takes place it seems logical to consider the use of anticoagulants. The relationship between ischæmia and hypertension is established as the precursor of cerebral as well as renal lesions. Presumably arterioles go into spasm as a reaction to heightened blood pressure and it is not therefore unreasonable to attempt to lower blood pressure by the exhibition of the hypotensive drugs now available. This

procedure must be pursued with caution, because too rapid and too great reduction will diminish the pressure required to maintain the patency of the arterial system. Reserpine, which is slow acting and moderate in its hypotensive effect, is preferable to the more active ganglion-blocking agents. After the development of frank thrombosis, the treatment of the patient is the same as that of the paraplegic (see p. 812) Subsequently, residual disturbances such as hemiplegia and dysphasia require the treatment described elsewhere (see p. 833). If after recovery the use of anticoagulants is favoured, effective preparations should be given under strict control without intermission for a matter of months or even years. When hypertension is present, the administration of a drug such as reserpine may be indicated. Again, treatment should be continuous unless side-effects such as mental depression occur. Blocking or extirpating the stellate ganglion has no therapeutic effect. A history of cerebral thrombosis is an absolute contra-indication to any operative interference with the sympathetic nervous system in cases of hypertension. In the larger cerebral arteries sudden occlusion with thrombosis occurring in the course of progressive vascular disease gives rise to extensive infarction of the brain and simulates the pict[illegible]

is fi[illegible]
As the use of anticoagulants has become a matter of routine in such cases, it is well to remember that embolism may follow the withdrawal of such therapy. Prophylaxis of cerebral embolism is, therefore, dependent to some extent on protracted anticoagulant treatment applied to the management of coronary disease. In the younger age-groups embolism from a cardiac source is usually due to dislodgement of an auricular clot when the mitral valve is stenosed. Prevention of this complication may be achieved by valvulotomy in a suitable cas[illegible]
of [illegible]
em [illegible]
em [illegible]
of [illegible]
Emboli arising from the lung and passing through the left side of the heart are usually infected

Cerebral Arteriosclerosis.—In this condition changes in the blood vessels are slowly progressive and seldom give rise to the dramatic events of thrombosis and hæmorrhage. The clinical picture is one of progressive dementia making its own peculiar demands and ultimately requiring institutional care.

[illegible]

encephalopathy are an expression of the height of the systemic blood pressure, the critical diastolic level being about 140 mm. Hg. or more. Hypertensive encephalopathy is a serious emergency; not only may grave permanent effects such as blindness, paralysis and aphasia result, but the condition if untreated may prove rapidly fatal. Since it is known that the condition is due to heightened systemic blood pressure, reduction of that pressure is the first requirement in treatment The drug of choice is that commonly used to produce hypotension

during anæsthesia Arfonad in ampoules of 5 ml. containing 250 mg. is available for intravenous injection Doses of 25 mg to 100 mg. will depress the blood [illegible]

vascular spasm Subsequent measures to prevent recurrence are those adopted in the treatment of hypertension (see p 584)

THE DEMYELINATING DISEASES

Disseminated Sclerosis.—Assessment of the value of treatment in disseminated sclerosis is always uncertain because of the tendency for symptoms to remit and exacerbate whether or not the patient is treated It seems clear, however, that the most important single factor in handling cases of this disease is avoidance of fatigue. Once the diagnosis has been made, complete rest should be ordered in any acute phase of the illness, and only when symptoms are static should the patient be allowed to return to work During phases between exacerbations it is important that work should be well within the physical capacity of the patient. The frequency with which exacerbations occur after periods of physical exhaustion is sufficiently striking to emphasize the importance of such advice. Anxiety also takes physical toll of the patient and he should [illegible]

[illegible] of a certain amount of physical exertion he must not engage in occupations or diversions likely to cause injury It is extremely difficult to impose such a regimen on people who have only experienced an attack of retrobulbar neuritis or transient diplopia. Far too often, however, such incidents are followed by sudden disabling symptoms of palsy, inco-ordination and sensory defect. The measure of rest must, of course, depend on the extent of involvement of the nervous system in the acute phase If the acute exacerbation is seriously disabling, the patient should be treated by three months' rest in bed Symptomatic improvement does not justify shortening this period of time

There is, of course, a considerable difference between the management of the acute phase of the disease and that of the chronic slowly progressive disorder. In the latter state everything must be done to restore the patient's [illegible]

So far none of them has proved effective Nevertheless there is no doubt that patients with disseminated sclerosis should be given some form of drug treatment if only for its psychological effect The particular medicine given should not have side-effects and should not be expensive

A great deal has been said in the past about the termination of pregnancy in women who are suffering from the disease. There is no evidence that the completion of pregnancy has an adverse effect on prognosis; indeed more harm is done by terminating pregnancy than by allowing events to run their course

Neuromyelitis Optica (*Devic's Disease*).—This demyelinating condition is a separate entity distinct from disseminated sclerosis. Bilateral retrobulbar neuritis occurring first in one eye and then the other within a period of days is characteristic of the early manifestations of the disease occurring months before signs of a transverse lesion of the cord appear. Alternatively, the spinal lesion may sometimes precede the bilateral retrobulbar neuritis. There is a tendency for the symptoms ar[illegible]
bulbar neuritis may [illegible]
that irreversible cha [illegible]

PROGRESSIVE MUSCULAR ATROPHY AND AMYOTROPHIC LATERAL SCLEROSIS

Nothing is known to influence the downward course of this condition. Treatment with amino acids is based upon faulty evidence and is a waste of money. Vitamin E is no more effective. Local stimulation and massage are contra-indicated The patient should be encouraged to indulge in moderate [illegible]

condition is so depressing and the outlook so hopeless that it does not seem worth while prolonging the patient's misery.

CONGENITAL AND FAMILIAL DISEASES

Friedreich's Ataxia.—The commonest familial ataxia is Friedreich's disease. A great deal can be done by re-educative exercises to combat incoordination as in the case of tabes dorsalis. The patient is taught to use his eyes in compensating for the loss of proprioceptive sensibility. There is no drug which has any effect on the course of the disease.

Congenital Cerebral Palsies.—See p 839.

EPILEPSY

[illegible] understanding of [illegible]

Every effort must be made to prevent two such people from mating. On the other hand, when epilepsy occurs as an isolated instance in one member of a family, the chances of that individual producing an epileptic child by a normal person with no family history of epilepsy are no greater than that of two normal persons having an epileptic child. Sometimes advice against marriage rests primarily upon economic circumstances, depending upon employability and earning potential. Frequent attacks difficult to control by anticonvulsant drugs,

and the presence of mental deterioration in spite of treatment, are further contra-indications to marriage. When epilepsy is a manifestation of trauma, vascular disease, syphilis, inflammation or tumour of the brain, it does not of course carry with it a hereditary stigma

Occupation.—For the sake of the patient's own safety and for the safety of other people, prohibitions have to be imposed on the epileptic When an individual is liable to have an epileptic seizure he must not drive a car. The legal position with regard to this is ill-defined. Many epileptics apply for driving licences and obtain them largely because specific inquiry into their fitness to drive is loosely worded and under-emphasized in the application form

It is extremely difficult to know where to draw the line When applying for a driving licence, the epileptic, having admitted the occurrence of bouts of unconsciousness, may, after seeking professional advice, be considered capable of driving because adequate treatment and the infrequency of attacks have rendered the risk of a seizure while driving remote If the doctor says the patient is capable of driving, there is no onus placed on the Licensing Authorities—the onus is on the doctor. The view has been held, with some justification, that the history of an epileptic seizure should debar the individual from driving for life If this view is pushed to its ultimate conclusion, then the history of convulsions in infancy would disqualify the potential driver When a man, having had an epileptic seizure, depends on driving a car for his livelihood, a certain amount of hardship is caused by preventing him from continuing. Nevertheless, if the possibilities in most instances are appreciated, the prohibition should be ruthless in spite of all attempts at persuasion. This prohibition should not, however, be absolute. If a man has been free of epileptic seizures for a period of six or seven years, the risk of accident in driving a car is minimal Indeed, the risk is much less than from the intoxicated or drugged motorist or from one severely physically handicapped, whether the disability be due to trauma, to primary disease of the nervous system or to cardiovascular disease.

Occupations which involve potential danger to the individual and to others should be forbidden the epileptic He should not work in heavy industry among machinery; he should not risk working at a height from which he is liable to fall, nor can he be entrusted with the control of any mechanical device such as a crane, in the operation of which serious damage would occur if consciousness were suddenly lost Perhaps the most important prohibition so far as recreation is concerned is in swimming, which should be absolutely forbidden.

Grand Mal Epilepsy.—The simple measures for controlling the patient in a grand mal seizure are well enough known and merit only the briefest consideration. Of primary importance is to ensure that the upper respiratory passages are free Thus it is absurd to waste time removing the collar from a man in a fit when his denture has been broken and is lying at the back of his throat, or when his tongue has fallen back to obstruct his larynx. In so far as is possible, the limbs should be prevented from striking surrounding objects, particularly fires and radiators. It is advisable to place some form of gag between the teeth—a spoon with a padded handle does well to prevent laceration of the tongue. If, however, the teeth are clenched and the tongue is not bitten, it is better not to interfere. When the tonic and clonic phases have ceased and the patient lies in a flaccid state, mucus should be removed from the back of the throat by swabbing and the head should be turned to one side with the angle of

the jaw pushed forward so that the tongue does not slip back. The epileptic should use a hard pillow during the night, as he may turn over in a seizure and smother himself in a soft one.

Drug Therapy.—Bromide has now no place in the treatment of epilepsy; indeed it is doubtful if the use of bromide in any condition is justifiable. The frequency with which bromide intoxication causes a confusional psychosis requires emphasis. Phenobarbitone is the sheet anchor in the treatment of epilepsy. It has two merits—it is cheap and it is effective. Most epileptics can be controlled by phenobarbitone alone; only when the patient takes seizures in spite of a maintenance dose of 0·2 g. (3 gr.) per day should other measures be considered. Secondary to phenobarbitone therapy is treatment by the hydantoinates, of which the most important is phenytoin. In the resistant case, when a maintenance daily dose of 0·2 g. of phenobarbitone is proving insufficient, 0·1 g. (1½ gr.) of phenytoin morning and evening should be added. Sometimes the combination of these two drugs acts better than either drug alone in increased dosage. On this assumption pharmaceutical manufacturers have produced capsules containing both phenytoin and barbiturate. It is strongly recommended that these expensive combined preparations should not be used. This advice is given for two reasons—it is simple to alter the dosage of either drug when that dose is known and when the drugs are given separately, and, further, it is very easy to forget the relative amounts of each drug in any given combined preparation.

Occasional untoward effects result from phenobarbitone and phenytoin. Some people are rendered drowsy by small doses of phenobarbitone; the giving of amphetamine to counteract this diminishes the anticonvulsant properties of phenobarbitone. In these cases it is advisable to try phenytoin either alone or in combination with primidone (see below). Rashes sometimes result from barbiturate administration; if they occur, alternative therapy should be given. Toxic effects, even after the prolonged administration of phenytoin, sometimes develop very rapidly. These are blood dyscrasias, double vision, giddiness, vomiting and ataxia Under such circumstances the administration of the drug should be stopped forthwith and replaced by enough phenobarbitone to make the patient drowsy. Some hypertrophy of the gums is to be expected in most cases undergoing treatment by phenytoin, but this does not constitute a contraindication to the use of the drug.

Primidone (Mysoline) is an important addition to the therapeutic armamentarium in the treatment of epilepsy It should not be used as the initial treatment but reserved for those cases which are not satisfactorily controlled by phenobarbitone and phenytoin. Under such circumstances primidone should be introduced gradually either in addition to the previous maintenance therapy or substituted for the phenobarbitone. The drug should be used with care, for idiosyncrasy to it is not uncommon and may result from a single isolated dose of 0·25 g. The symptoms are intense giddiness, vomiting and drowsiness. Occasionally these symptoms may disappear with persistent administration of the drug, but if adaptation to the administration of primidone has not occurred within a period of three days it may be taken that the patient will never tolerate it. If the patient tolerates primidone, the drug should be gradually substituted for phenobarbitone in the first instance and later perhaps for the phenytoin Control is a matter of trial and error, some people do best on primidone alone, with ultimately a daily dose of 2 g. Other people do best on a combination

of phenytoin, 0 2 g., and primidone, 1 5 g., daily. When larger doses prove necessary, the patient usually requires to be in hospital or in an epileptic colony. The use of other anticonvulsant agents is not recommended as a routine in general practice.

On no account must absence of seizures lull either the physician or the patient into a false sense of security Once appropriate maintenance therapy has been established, this should be continued over a period of at least two years before considering a reduction of the daily dose of anticonvulsant. When seizures occur cyclically at the time of menstrual periods, it is advisable to give a little more phenobarbitone for a day or two before, during and after the period.

In spite of the most careful treatment a small minority of epileptics degenerate mentally, rather from the nature of their central nervous disorder than from the administration of drugs Nothing can be done to prevent this As there is a relatively high incidence of epilepsy in the mentally defective, it is important to realize that mental defect may be the major disability If this be the case, institutional care is required (see p 841)

Petit Mal.—Treatment must depend upon the accuracy of diagnosis. All patients thought to have petit mal should be subjected to the investigation of electro-encephalography This is important because many patients show the typical spike and wave electrical activity characteristic of petit mal without any of the irregular paroxysmal dysrhythmic patterns of a grand mal type. A very large number of cases, however, show both electrical disturbances. The reason for such discrimination as a prelude to therapy rests on the generally accepted view that drugs which act as anticonvulsants in petit mal may aggravate grand mal both in the frequency and in the intensity of the attacks. In the great majority of cases it is inadvisable, therefore, as a first approach to give troxidone, which is the drug indicated in the treatment of petit mal, without protecting the patient against the grand mal attack by giving in addition phenobarbitone or its equivalent Generally speaking, petit mal is much more resistant to treatment than grand mal As troxidone has occasionally dangerous side-effects such as granulocytopænia, it is wise to consider simpler therapy. Some cases are benefited by using belladonna in conjunction with phenobarbitone. There is no official preparation combining belladonna and phenobarbitone, and probably the cheapest and best preparation to use is the proprietary Belladenal, which contains 50 mg (¾ gr.) phenobarbitone and 0 25 mg ($\frac{1}{250}$ gr.) belladonna leaf per tablet If this fails in a dosage of four tablets daily, combined therapy with troxidone and phenobarbitone should be substituted. Troxidone is available in 0 3 gr. tablets, and one should be given two or three times a day to children and up to six times a day to adults. A careful look-out must be kept for the signs and symptoms of agranulocytosis The skin must also be carefully watched because exfoliative dermatitis is a dangerous and not very uncommon complication of treatment The glare phenomenon is perhaps uncomfortable but is no contra-indication to the use of the drug

Psychomotor Epilepsy.—Disorders of behaviour with complete amnesia may be epileptic in origin but have to be carefully differentiated from the automatisms of the hysterical fugue and from the amnesic extravagances of intoxications. When such states are manifestations of epilepsy they are difficult to control, only trial and error with the drugs already mentioned will show whether it is possible to modify the pattern of the attacks. Occasionally some violent action by an epileptic patient may land him in the criminal courts, which

have no therapeutic jurisdiction beyond detention until Her Majesty's pleasure be known. Such cases should be under restraint in a mental hospital pending a possible surgical attack on epileptogenic focus in the temporal lobe.

n dealing with this in 5 to 8 ml. dose sive seizures, there should be no hesitation in seeking the aid of an anæsthetist. When no such

soon as the seizures abate. Enemata of 8 to 16 ml. (2 to 4 fl. dr.) can be repeated at two- to four-hourly intervals depending on the severity and number of subsequent fits. The onset of hyperthermia (see p. 809) is a real danger in status epilepticus. The greatly increased metabolism resulting from the seizures raises the temperature to such a degree that the thermal regulatory functions of the hypothalamus are impaired.

MIGRAINE

The treatment of migraine consists in avoiding the precipitating causes of an attack if they are known. Any error in refraction should be corrected; over-fatigue, physical and nervous, and indiscretions of diet should be avoided; disease of the accessory nasal sinuses should be treated; if there is a history of dyspepsia and flatulence, the gall-bladder function should be investigated and, if disordered, treated

the attack occurs. More severe cases of migraine do not respond to a simple powder of this kind, and the only relief possible may be from ergotamine tartrate by subcutaneous injection in a dose of 0·25 to 0·5 mg. The patient should be taught to give the injection himself. The dose may be repeated within an hour. Milder cases respond to ergotamine tartrate by mouth. When taken orally the dose is 2 mg, which can be repeated in one or two hours; the drug should be dissolved under the tongue. Sometimes attacks of migraine occur daily and require a maintenance dose of 2 mg nightly.

Urea has been recommended for the treatment of migraine. It is certainly

It should be remembered that the migrainous attack is often precipitated by emotional causes, the pattern of which is repressed resentment.

VERTIGO

Vertigo of labyrinthine origin is a disabling and alarming symptom and carries with it symptoms of psychological stress. When attacks are frequent the patient should be given as a routine 1 g. (15 gr.) of ammonium chloride in tablets of 0·5 g thrice daily for periods of three days, alternating with periods

of three days' rest from the drug Salt in the diet should be restricted. This treatment is designed to reduce endolymphatic pressure

It is noteworthy that many sufferers from migraine find that their symptoms disappear about the age of forty, only to be replaced by labyrinthine vertigo. Acting on the assumption that the two conditions have something in common, ergotamine tartrate, used as in th[illegible] treatment of migraine, may be found helpful. Antihistamine drugs merit a tr[illegible] [illegible] in 25 mg. doses is finding increasing favour in treatment, [illegible] D[illegible], probably the safest of the non-mercurial diur[illegible] [illegible] future therapy. The latter drug should be g[illegible] every second or third day

In intractable cases the surgical procedure of sectioning the eighth nerve in the posterior fossa may be carried out, provided the disturbance can be traced to one internal ear, and provided the other ear is intact

DISORDERS OF MUSCLE AND THE MYONEURAL MECHANISM

MUSCULAR DYSTROPHIES

There is no satisfactory specific treatment for the muscular dys[illegible] The therapeutic use of glycine arose from the idea that ingestion of [illegible] might spare muscle by providing readily available protein There is no [illegible] that such treatment can either reverse or arrest the dystrophic process. [illegible] assumption that a vitamin deficiency might be present, α-tocopherol [illegible] has been tested and found wanting Deformities and contractures [illegible] prevented by exercise as long as the patient is able to execute the nece[illegible] ments, and by passive movement when the limbs become immobile [illegible] of these slowly degenerating patients involves many problems [illegible] of treatment is to provide them with work under protected con[illegible] to their limited capacity

DYSTROPHIA MYOTONICA

(Myotonia Atrophica)

No specific treatment can arrest or modify the course of th[illegible] [illegible]luence exerted by drugs is purely symptomatic in effect Th[illegible] [illegible]ne and slowness of movement can be reduced by giving [illegible] [illegible]uinine bihydrochloride once a day Lenticular cataract, an [illegible] [illegible]nent to the muscular disorder, can be dealt with by the oph[illegible] [illegible]here is no further abnormality in the refractive media or in th[illegible]

MYOTONIA CONGENITA

Myotonia congenita is a muscular disorder similar to [illegible] atrophica; it is treated in the same way

MYASTHENIA GRAVIS

The response to treatment in myasthenia gravis is var[illegible] neutralize the effect of cholinesterase by the administ[illegible] effective analogue neostigmine In most

1 mg. of neostigmine has the dramatic effect of improving the myasthenic condition, sometimes achieving complete normality within fifteen minutes. Neostigmine should be given with atropine, 0 4 mg. ($\frac{1}{150}$ gr.) of atropine sulphate, to prevent vagal effects—intestinal colic, cardiac inhibition and sweating. Administration of the atropine should precede that of neostigmine by half an hour. Neostigmine, fortunately, is active by the mouth and 15 mg. tablets are available for maintenance treatment. Eight to sixteen of these tablets can be given during the course of the day. Every possible care should be taken to see that the maintenance dose of neostigmine is continued. Some cases of myas-

to neostigmine are 1·3 g. (20 gr) of potassium citrate and 30 mg. ($\frac{1}{2}$ gr.) of ephedrine three times a day. In the resistant case the use of these drugs in combination with neostigmine is desirable. When the muscles of deglutition are so weak in the ... less, the sub-cutaneous injection

Pyridostigmine ... eostigmine in maintenance treatment The dosage is four times that of neostigmine and therefore pyridostigmine has been made available in 60 mg. tablets for oral administration. The drug's action is slower and more prolonged than that of neostigmine; it is therefore peculiarly suitable for use at night in those patients whose symptoms are severe on waking in the morning.

Because of the very high incidence of thymic tumours in myasthenia, the operation of thymectomy has been introduced even for cases in which no such tumour can be demonstrated. The procedure would be a formidable one for a normal person and is naturally more serious for a myasthenic. It should, therefore, only be contemplated when the general condition of the patient has been

greater or less degree of improvement may be anticipated in a proportion of cases, and in a few this improvement is dramatic. The operation is most likely to be successful in young patients with a short history of the disorder in whom the myasthenia is generalized rather than confined to a localized group of muscles Some improvement has also been occasionally observed when X-radiation has been applied to the region of the thymus

FAMILIAL PERIODIC PARALYSIS

This rare disease has no specific cure, but symptomatic relief is afforded by the administration of potassium chloride in 3 g. doses This salt can be given just before retiring, and in the morning if the patient is paralysed on awakening. The action of the potassium is to increase neural and muscular irritability.

NEURITIC SYNDROMES

Peripheral nerves may be damaged by mechanical causes, by infections and by toxins, endogenous and exogenous. They may degenerate as the result of specific nutritional deficiency or as the result of diminished blood supply *In*

addition there is an ill-defined group of distressing, painful conditions conveniently, perhaps ignorantly, described as neuritis of rheumatic origin.

Paralysed muscles must be protected from overstretching by appropriate splinting. Experimental work has shown that denervated muscle does not lose bulk as rapidly when effective daily electric stimulation is given. Electrical stimulation should therefore be carried out as soon as the pain of stimulation can be tolerated. The paralysed limb should be moved passively through as full a range of movement as possible. This need be done but once daily to prevent contractures and fixations secondary to immobilization When muscles are recovering, exercises designed to bring them into play should be prescribed. Massaging paralysed muscle is valueless and has no scientific justification. Fixation of a limb, however, carries with it secondary vascular effects. The skin becomes cold and discoloured and at times œdematous These changes are lessened by effleurage, consequently the nutrition of the skin may be helped by that form of massage.

TRIGEMINAL NEURALGIA

Paroxysmal trigeminal neuralgia, or tic douloureux, is characterized by such exquisite pain that its relief earns embarrassing gratitude Milder cases respond to 0·6 ml (10 min) of the tincture of gelsemium thrice daily No radical measures should be undertaken when simple analgesics and mild sedatives are sufficient to control the symptoms until a natural remission occurs On the other hand the pain may be so severe and so frequent as to drive the patient to suicide. Such desperate pain demands desperate treatment Operative interference by differential section of the sensory root of the trigeminal nerve or the more recent procedure of decompression of the Gasserian ganglion (Tarnhoj) merits consideration. These operations are remarkably free from risk in the hands of a competent neuro-surgeon who discriminates in his choice of cases It is doubtful if the older procedures of alcohol block of either the second and third divisions as they emerge from the base of the skull are justifiable nowadays except in the attempt to abolish the pain of malignant disease of the face or tongue. There is still a place, however, for two minor procedures using alcohol as a blocking agent When the pain is confined to the region of the infra-orbital nerve or to that of the inferior dental nerve, the respective nerves may be destroyed at the infra-orbital foramen or the mandibular foramen

Lancinating, explosive pain in the face is not always due to tic douloureux. When teeth have been lost and the bite is overclosed, pain may arise from the region of the temporo-mandibular joint and be referred to the face, or it may be experienced deep in the ear and may radiate into the throat and tongue. Agonizing pain is precipitated by eating or speaking The cure is the prosthetic procedure of supplying dentures of sufficient depth to avoid traumatization of the jaw joint and backward pressure on the thin tympanic plate

HERPES OF THE FIFTH CRANIAL NERVE

This distressing condition may give rise to much disfigurement and pain. During the acute phase the skin should be kept dry and dusted with a simple dusting powder The compound of aspirin, phenacetin and codeine usually alleviates the pain in the acute phase, though occasionally it is so severe as to require morphine Post-herpetic neuralgia is a baffling sequel. The actual pain is so disagreeable that the sufferer develops a neurosis more difficult to

treat than the pain. Application of nupercain ointment, ½ per cent, gives some relief by reducing the cutaneous stimulation which facilitates spontaneous pain. Operations on and injections into the Gasserian ganglion or its roots are ill-advised; the condition usually subsides spontaneously in the course of time. The most intractable post-herpetic neuralgia usually occurs in the first division of the trigeminal nerve. The site of pain suggests to the sufferer that some serious disease is present within the skull itself; he believes the gravity of the disturbance must equal the severity of the symptom. Assurance must go hand in hand with any physical or medicinal treatment. Ulceration of the cornea is another unfortunate sequel of the acute attack of herpes of the first division of the fifth cranial nerve. The problem concerns the ophthalmologist, who should always be consulted when the cornea is damaged.

BELL'S PARALYSIS

The majority of cases recover spontaneously without any special treatment. Counter-irritation applied over the region of the stylo-mastoid foramen has little to commend it For the milder case with little loss of muscle tone and showing early signs of recovery, exercises in front of a mirror are sufficient Lax and grossly paralytic facial muscles require splinting and electrical stimulation. The actual splint takes the form of a rubber-covered wire bent to form a " U " at one end and a spectacle leg at the other. The " U " bend hooks into the paralytic angle of the mouth and the spectacle leg fits over the ear to exert traction on the angle of the mouth and so to restore facial symmetry. Electric stimulation should be continued until the patient is able to undertake voluntary movement before a mirror. The idea that the so-called post-paralytic contracture of the face is due to electrical treatment is totally unsound. The contracture occurs because of random regeneration of the facial fibres after a pathological process has destroyed the fascicular pattern of the nerve. Nothing can be done to correct the results of random regeneration. Should no regeneration occur, medical treatment is of no avail and the patient should be referred to a plastic surgeon for the insertion of a fascial sling. In all cases of facial paralysis of the lower motor neurone type accompanied by defective corneal sensation, the eyelids on the affected side should be stitched together.

COSTO-CLAVICULAR SYNDROMES

Congenital abnormalities in the region of the neck and the thoracic outlet may be symptomless for years. When the tone of the muscles of the shoulder girdle is lowered from whatever cause, symptoms referable to the arms make their appearance in the presence of previously symptomless congenital abnormalities. Treatment of these syndromes is primarily medical. If the syndrome is developed through excessive work, e.g. lifting heavy loads, rest is the first essential. Rest will permit the distorted neural structures to recover, with recovery, symptoms disappear.

If the patient has lost his muscle tone through debilitating illness, convalescence from that illness has not been sufficient and further rest must be prescribed. After alleviation of pain and paræsthesiæ by means of rest, exercises calculated to restore muscle tone to the shoulder girdle should be instituted Under no circumstances should surgical intervention take precedence over these simple measures Indeed, such operations as removal of cervical ribs and cutting

of scalene bands are seldom necessary. Although they may remove symptoms, they do not deal with the precipitating cause of the complaint.

MUSCULO-SPIRAL PARALYSIS
(*Saturday-night Palsy*)

This is best treated by resting the extensors of the wrist and fingers in a cock-up splint If the paralysis is profound, electrical stimulation of the affected muscles should be carried out assiduously Whenever voluntary power begins to return, remedial exercises should be instituted.

TRAUMATIC ULNAR NEURITIS

In subjects with a wide carrying angle and hyperextensible elbows, the ulnar nerve is mobile and easily dislocated from its bed in the epicondylar groove. Because of this anomaly the nerve is liable to injury from pressure at the elbow. In some occupations pressure on the ulnar nerve at the elbow can scarcely be avoided. Treatment is directed to removing the cause by instructing the patient about these postures which render the ulnar nerve liable to pressure. If these causes can be removed, further treatment may be unnecessary. When the ulnar nerve is thickened and mobile at the level of the elbow, prevention of trauma in everyday life may be impossible Under such circumstances satisfactory results follow transposition of the nerve from the epicondylar groove to the anterior aspect of the forearm Burying the nerve in the head of the flexor-pronator group of muscles is an additional protection Weakness and atrophy of the intrinsic muscles of the hand should be treated by exercises and appropriate occupational therapy.

MEDIAN NERVE PALSY

Recently an affection of the median nerve has been described as the carpal tunnel syndrome. The symptoms are produced by pressure on the nerve as it travels *under cover of the anterior carpal ligament The recommended procedure* of cutting down on the nerve at the site of the lesion and freeing it in its bed should be tried only after rest has failed. Prevention of relative movement between the nerve and the tissues surrounding it will permit œdema and [illegible] therefore, should be to [illegible] often effective without [illegible] and paræsthesiæ have disappeared after rest, passive movement and exercises should be instituted

TRAUMATIC MEDIAN AND ULNAR LESIONS WITHIN THE HAND

[illegible]

HERNIATED NUCLEUS PULPOSUS

Among the causes of sciatica, retropulsion of an intervertebral disc takes first place. The high incidence of herniated discs in cases of lumbago and sciatica does not alter the fact that most patients were cured spontaneously before herniations were recognized. Once the diagnosis has been established,

rest in bed should be ordered. Fracture boards are placed under a hair mattress and only one pillow is allowed. The patient may be permitted to roll on to either side. He is not permitted to sit up; his spine must be kept as nearly horizontal as possible. Bed-pans and urinals are part of the routine. After or during the third week of this treatment, exercises in bed are ordered; these are graduated and the patient is allowed up at the end of the third or during the fourth week. The whole object of treatment is to prevent relative movement between the herniated disc and the affected nerve root. The affected root is œdematous, and œdema and pain are perpetuated as long as relative movement occurs. With rest, the œdema disappears and the root adapts itself to the

ment precipitates the condition Indeed, some recommend rest in hyper-

usually adequate to alleviate the pain.

The small percentage of cases not responding to the treatment indicated require to be dealt with surgically by removal of the offending protrusion, as are those few in whom paralysis is marked. When paralysis is extensive, the earlier the operation is undertaken the better.

That terror has its physical counterpart in increased muscular tension. The patient shuns all movement of the spine, fearing to cause permanent damage to it or to his nerves Assurance must be given of the stability of the spine and of the forces which protect it against damage. Much residual pain is caused by local spasm of muscle brought about by fear, and that fear must be allayed.

SPEECH THERAPY

acquired in maturity. Their lot is scarcely less difficult; they are hampered in all self-expression by word of mouth. Not merely the number afflicted but the magnitude of the individual problem make the need for speech treatment clamant.

Too often in the past the sufferer has been exploited by quackery at the hands of the unqualified. Today the speech therapist is an officially recognized medical auxiliary; her special training in normal and disordered speech, relevant anatomy and physiology, psychology and educational method fit her to tackle the problem

Speech clinics have now been established at the main teaching hospitals and the treatment of children is part of the school health service.

The selection of patients for the speech therapist depends on the cause of the defect and the outlook for the individual. Cases of dysarthria from bulbar

An adequate account of the condition from the practitioner's angle should accompany the patient. This obligation should be reciprocated by the therapist, who in return should seek guidance from the doctor in the management of the case.

The methods used by the therapist vary with the cause of the defect. In deformity of the upper respiratory tract, treatment is directed towards producing the best articulate sound consistent with the deformity, by exercises in the use of a limited speech equipment

The spasms and tics of stuttering demand exercises in progressive relaxation of the whole voluntary musculature. These exercises combat spasm in the muscles of articulation and rid the patient of that general muscular tension which is the result of emotional strain. In complete muscular relaxation, for some unknown reason, the storms of psychological conflict abate and the mind responds more readily to suggestion and instruction. Because the dysphasic patient is rendered worse by emotional stress, relaxation therapy becomes an important means of helping him

Intellectual speech difficulties caused by lesions of the dominant hemisphere make greater demands on the skill and experience of the therapist She has to use educational technique to facilitate activity over the associative pathways remaining intact The patient is made to associate various sensory experiences of one object with another and with the appropriate word symbol Patients with inferior cerebral equipment have to go back to learning language afresh.

WRITER'S CRAMP

treatment is required in both—clearing the distorted emotional background,

PHYSIOTHERAPY IN NERVOUS DISEASE

No consideration of treatment of neurological conditions would be complete without some discussion of physical methods of treatment These physical methods are massage, heat treatment, electrical therapy and exercises, remedial and re-educative

Massage.—Massage was once the physiotherapist's obsession, and dearly has the physiotherapist paid for harbouring it. The devotion to the belief in the efficacy of massage prejudiced the whole natural evolution of more useful and rational physiotherapy. A legitimate use for massage may possibly be found in the treatment of muscular spasm.

Most people can produce pain by sitting stiffly in an awkward position; this being true, it would be surprising if the constant increase in muscular tension, so characteristic of the anxiety state or of many organic diseases, did not cause pain In this type of case, massage may be of some service in the achievement of muscular relaxation.

Massage is also of some value in the treatment of those cutaneous vascular disturbances which depend on poverty of movement of a limb. Rubbing will increase blood flow through the skin vessels and may prevent the formation of ulcers and sores. This treatment should be applied only to limbs with a motor defect and not to those with disturbance in cutaneous pain sensibility. Massage can make no claim to increase the blood flow through muscle nor to improve any defect in muscle innervation. Blood flow through muscle is a function of its activity in contraction, and the physiotherapist's first concern, when trying to improve the nutrition of atrophic muscle, is, if possible, to make that muscle contract by any means at her disposal.

Heat.—Heat can be given in many ways The infra-red lamp is an adequate source of penetrative heat, but its benefits are often purely psychological. Beyond question a hot bath is much more efficient There is some justification for the use of the hot-wax bath, the thermal capacity of wax is not so high as that of water, but wax treatment is kinder to the skin than is prolonged immersion in hot water. Short-wave diathermy is efficient in heating deeper structures, but, as a rule, should not be used for increasing cutaneous circulation It must be emphasized that care should be used in the selection of cases for heat treatment Patients suffering from trophic lesions with sensory impairment should usually be excluded as the normal axon protective reflex is lost in such cases.

The main value of heat therapy in neurological conditions is to improve cutaneous circulation in paretic limbs which are seriously impaired in movement but without sensory change A subsidiary use of heat therapy is to induce relaxation of voluntary muscle, this is of use in resting the hypertonic muscle of extrapyramidal disease, but at the best the effect is temporary.

Electricity.—Stimulation of muscle by electricity is at once an important and powerful therapeutic agent without which no neurological service can claim full efficiency. Galvanic and Faradic currents are both used. Galvanic stimulation should be used only when Faradic fails to cause a contraction. These modes of stimulation should be employed in patients with weak, atrophic muscles from a lower motor neurone lesion. Their use in any other type of lesion is to be condemned Good as the results may be in some lower motor neurone disorders, not all disease with lower motor neurone signs should be treated in this way The treatment should be applied only when the process offers some hope of regeneration. To submit cases of progressive muscular atrophy or of myopathy to electrical stimulation is foolish and harmful. Electrical treatment properly administered is time absorbing. Daily stimulation should be attempted and each muscle under treatment should be made to contract ninety times at each session Such a course makes electrical therapy worth while, and that is why wasting time on valueless physiotherapeutic

measures is to be condemned. It should be remembered, however, that when a muscle is very weak the pain of an effective stimulating current may not be tolerated. Effective stimulation with a reduced current causing less pain is possible if the resistance of the overlying skin is reduced by scrubbing with a small nailbrush until it is red In a fresh case of anterior poliomyelitis, as soon as electric stimulation can be tolerated, contractions in weak muscles must be induced daily.

Little need be said of other forms of electric treatment Faradic baths may be of some use in the treatment of intrinsic atrophy of the hand as focal stimulation is often difficult and impracticable Sparking devices and baths with weak sinusoidal currents have nothing to commend them

Exercises.—Exercises are of first importance in physiotherapy and indeed in medical treatment generally Graduated exercises of all kinds help the patient from early convalescence to full fitness for his former occupation True exercise is remedial and re-educative

Remedial Exercises.—These movements are executed by the patient voluntarily under the instruction of the physiotherapist They are divided into various types. Static exercises can be performed even when the patient is encased in plaster A little instruction and demonstration are needed to show the patient how to brace muscles without moving one part of the body relative to another. These exercises are the clinical equivalents of the isometric contractions of the physiologist Static exercises can be carried out against resistance applied by the therapist. In cases of inflammatory disease or trauma when relative movement of individual parts of the limbs or body might do harm, these static exercises are of great value in preparing the way for the exercises of movement against a load. Not only do these preparatory exercises pave the way for more strenuous activity but they increase metabolism and afford a sense of well-being otherwise denied to the immobilized patient

From the foregoing it can be seen that remedial exercises fall naturally into two classes: those which keep up the general muscular tone and stimulate metabolism, and those which are specially designed for the treatment of articular muscle groups Those exercises concerned with the increase of eneral muscle tone have been described, and in this class breathing exercises also most important. In the second group voluntary movement of specific muscle is encouraged The efficacy of these measures may be increased when the patient is asked to perform a specific movement in manipulating apparatus pecially designed for the particular movement For example, in peripheral erve injuries and in polyneuritis, the flexors and extensors of the hand may be ade to move effectively by compressing and releasing a bulb such as one finds on a sphygmomanometer The next stage might be the use of spring dumb-bells. For movements of pronation and supination the "wrist-roller" is the appropriate apparatus For movements of extension and flexion of the foot there is no more effective exercise than bicycle pedalling against an increasing load. For spastic cases, exercises in relaxation are recommended. From prescribed movements the patient progresses to the use of the walking machine. Later, tripod crutches give extra stability and can be manipulated if the arms and shoulder girdle are sound

One of the greatest developments in physiotherapy has been the use of the Guthrie-Smith apparatus. This consists of a double Balkan beam from which are suspended slings to support the limb under treatment. These slings may

be sprung or hung by inextensible cords. By this means many exercises, impossible in an ordinary bed, can be performed. The whole purpose of the apparatus is to take the load of gravity from the contracting muscle when the muscle is too weak to contract against that force By suitable posturing of the

the feet on predetermined positions on the floor. The usual apparatus is a mat in the form of a runner with footprints marked on the mat. The patient is instructed to place his feet accurately on the footprints Music encourages rhythm of movement to produce a more natural gait.

Physiotherapy in Certain Neurological Conditions

Tabes Dorsalis.—Treatment of tabes dorsalis has been considered elsewhere Instructions have been given as to the specific measures to employ in combating the infective process (see p 189) Important as these specific measures are, the ultimate success in treatment depends on re-educative exercises

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Only by assiduous re-education can the tabetic hope to recover facility of movement in walking. Much of this facility may be acquired by himself in the natural course of events, but systematic re-education makes compensation faster and surer. The tragedy of the tabetic so far as reasonable recovery of function is concerned is when his vision is impaired as the result of optic atrophy. Here there is little point in prescribing re-educative exercises because he has then no means of judging the position of his limbs relative to one another and to the surface on which he treads.

Subacute Combined Degeneration of the Cord.—The treatment of this disease has been considered elsewhere (see p 419). Emphasis has been rightly laid on the success of specific measures and the ultimate benefit to the patient of assiduous and constant treatment. Neurological signs, however seldom disappear completely and often residual symptoms remain These

end is the same as for the treatment of tabes dorsalis— ... placing exercises rhythmically performed By these re-educative exercises residual disability is lessened, limitations imposed by reversible change are narrowed and restoration to useful employment is hastened.

PHYSICAL TRAINING

Gymnastic exercises are useful in restoring convalescents from certain nervous conditions to full fitness. Selection of patients for physical training depends on two main factors—the nature of the disease, and the nature of the patient's former and intended employment The disease should have a good

fitness is necessary for the pursuits of a dock labourer than for those of a bank-clerk, unless the latter is an athlete as well The nature of the disease must be considered in conjunction with the patient's age and general physical state. The second point is concerned with the load likely to be put on the patient once he returns to a normal way of life

Post-concussional states are slow to recover and are an anxiety to patient and physician alike. The sufferer is afraid to exert himself, he is afraid to stoop; his anxieties multiply with the perpetuation of symptoms Graduated exercises in bed as soon as they can be tolerated begin the physical training. when the patient is able to be ambulant, exercises in the gymnasium or in the open are undertaken which should avoid stooping, later, full fitness can be achieved by vigorous muscular exertions performed to the command of the instructor. Physical training, practised in groups, has a considerable psychological value. If the instructor is well chosen, the results will often be astonishing.

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state permits Swimming is of immense value in the treatment of many cases with residual palsies whether from anterior poliomyelitis or other cause

J. B GAYLOR.

THE WELFARE OF THE DISABLED

AN EVER-GROWING REALIZATION of the problems of disabled and handicapped persons has led to the development of much voluntary and statutory aid. Such services as are available should be utilized to the full. General practitioner and specialist alike are often too occupied with diagnosis and immediate treatment to be concerned with ultimate social adjustment. The doctor may be sorry for his handicapped patient, because he feels himself *impotent to handle the social problem. Doubt about what* do to with an unhappy, idle invalid would diminish if he knew what steps to take

Statutory obligations are defined in two Acts of Parliament; the Disabled [illegible] (Employment) Act (1944) and the National Assistance Act (1948). In

[illegible]

education, recreation, financial assistance, housing and correction of grievances and injustices through false assessment These voluntary organizations have been in the van of social progress and have shown the way to the legislators Wisdom in legislation has taken care to avoid the creation of a mutual antipathetic attitude. The State does not hesitate to use facilities offered by voluntary bodies and, indeed, gives them financial support Nor does the voluntary [illegible] seek what statutory service may be available.

[illegible] in reference [illegible] erson who, on account of injury, disease or congenital deformity, is substantially handicapped in obtaining or keeping employment, or in undertaking on his own account work of a kind which, apart from his injury, disease or deformity, would be suited to his age, experience and qualifications." The Act does not exclude mental illness from its scope

To set the machinery of the various services in motion, the first step is official registration of the " disabled person ". This registration is effected at [illegible] and immediately puts an onus on the Ministry [illegible] settlement [illegible] he limits of [illegible] mental capacity for work. If this is impossible

[illegible]

Remploy factory or at some other place approved by the Ministry of Labour if a better alternative to either exists in the voluntary organizations, a niche is found for the employment of the patient outside the more *official framework* It has to be remembered that the Ministry of Labour will subsidize a man during vocational training for a period of six months, either in a recognized protected workshop or in an approved factory. This provision makes the creation of protected workshops a feasible proposition because the load of under-productivity of the trainee is balanced by subsidy. The D R.O. has the right of entry to any

hospital, and the liaison between the hospital and the Ministry of Labour is through the hospital almoner.

Efficient and worthy though the almoner and D R O. are, the work of resettlement cannot achieve its purpose unless the clinician is prepared to devote time and thought to the individual problem Every disabled person is an [illegible]

buff form (D P.1) for the purpose—the product of a compartmented mind. It seeks to cover every possibility, and the only human aspect of the document is a blank space for General Remarks The D R.O merits the fullest sympathy in his difficult task. He knows industry, but has to cull the medical aspect of a problem from ticks on this printed buff form It would be easier if a note or, better, an interview were given the D R O by the doctor. In busy general practice this may be quite impracticable, but the doctor should not hesitate to refer this patient to hospital, not only as a problem in general medicine but as a problem in social medicine; this cannot be done by a slovenly scrawl on the back of his visiting card.

Major disablements are those of the nervous system, such as congenital cerebral palsy, epilepsy, mental deficiency, blindness and deafness and acquired palsy or mental defect from a great variety of causes Heart disease, congenital and acquired, pulmonary disease and diseases of the muscles make not infrequent demands on the services available for resettlement

Congenital Cerebral Palsy.—The sufferer may be called a " spastic " or be said to suffer from Little's Disease or Cerebral Diplegia. Two main groups exist—those who are capable of being educated and those who are not Naturally the very lesion which causes palsy may cause mental handicap.

The educable, congenitally palsied child presents two problems, one in remedial treatment and the other in education No apology is made for the intrusion of the latter, because the two problems are inextricably bound together and neither is capable of independent solution What is the size of this problem? That question is difficult to answer because many cases are hidden away; some of the intelligent are so palsied that the poverty of their self-expression renders them idiots in the general appraisal; others with milder palsy are defective in intellect and the congenital palsy is scarcely noticed. Competent authority, however, estimates that in Great Britain almost 2,000 educable cerebral palsied babies are born every year. A minority of spastics can be trained to live a [illegible]

in spite of facility in the highest abstractive faculties of the mind.

When confronted with the problem of how to deal with a palsied child certain measures must be adopted. First, an assessment of the intelligence should be made. This may be difficult because the child may have so much inco-ordination and palsy as to make the spoken word unintelligible, the drawn line meaningless and the gesture inadequate. If the child is educable, and the

If not, the child should enter a residential school for the care of spastics or should travel from his home to a special school equipped to deal with both the educational and physical aspects of the disorder.

Treatment exploits the functional integrity of intact pathways through the nervous system to achieve appropriate reaction to specific stimulation. The palsied child, particularly if he is athetotic and inco-ordinate, cannot be expected to execute movement towards a specific end if his main concern is the maintenance of equilibrium. When unaided, his main effort is to maintain a static

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delicacy.

Therefore furniture designed to cancel ataxias and palsies must be used before attention can be directed to any skill or craft natural to the normal but arduous to the spastic child.

For the spastic, exercises in relaxation are necessary. Mimicry, that ready

may be bound up. Exercises in the gymnasium may be planned on an evolutionary analogy. Wriggling imitations of reptilian movement give place to copying the amphibian, to be followed by quadrupedal progression and primate activity. In this scheme the swimming pool is a useful adjunct to any school for spastics.

At all stages of training the orthopædic specialist may order braces, calipers or splints to correct deformity or to give support to weak limbs Only as a last resort will he use operative measures such as tendon section or nerve crushing.

Speech therapy plays an important role, equipping the spastic child for a life of independence. The therapist's task is twofold—to correct the disorders of articulation and to deal with defects in the appreciation and expression of language. In the former she is concerned with mechanisms and innervation of the muscles of the tongue, larynx, mouth and the respiratory apparatus as a whole, in the latter she is occupied with an educational problem—that of establishing patterns of activity at the highest levels of speech, the understanding and the utterance of language as a structure of symbols.

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pare the child for the special
school.

The following points may be of some help Education Authorities are required to accede to any reasonable request on the part of parents to examine any child who has attained the age of two years. The Authority is also obliged to provide special educational facilities in the case of mental and physical handicap and the Authority may require parents to submit any child requiring special care to a medical examination by their medical officer. In the case of

spastic children, if the Authority is unable to make necessary provision within the area for which it is responsible, it may make arrangements for training and treatment at a special residential school On the other hand, the family doctor or the specialist consulted may make direct approach to the special school and ask the Local Authority to bear the cost of training and treatment in that school. In Scotland the Scottish Council for the Care of Spastics has its own residential [illegible]

Epilepsy.—This condition, or rather symptom, constitutes one of the major concerns of those interested in the welfare of disabled people That this should [illegible]

[illegible] institutional care is required Of the remaining 17,500 epileptics, 8,000 are feeble minded, of whom 3,000 dwell in urban and 5,000 in rural areas. Thus, in Scotland 9,500 normally minded epileptics remain to be dealt with Of these roughly 20 per cent. have nocturnal seizures and do not constitute any great employment problem In round numbers, 7,500 people in Scotland are liable to have seizures at work and at play There is no evading the issue that an epileptic fit disturbs other people, sometimes even more than it does the victim of the seizure. The handicap prejudices employment and leisured occupation alike. Employers tend to exclude the epileptic from that quota of 3 per cent. [illegible]

[illegible]

ment of the epileptic is the Red Cross Treatment Centre. There the epileptic may find diversional therapy leading to more stable and remunerative employment. Certain industrial concerns have been able, because of interest and sympathy, to employ not a few who are liable to take seizures There is a great

need for educating employer and employees to accept the epileptic as being capable of achieving much that is up to normal standards of life and work When extreme difficulty arises because of ill-controlled seizures, the epileptic

There is a place also for hostels for epileptics. The epileptic who has no relatives and who is subject to nocturnal seizures with bed-wetting, irrespective of his liability to have fits during the day, is never readily accepted by any landlady no matter what his potential in industry or in a profession may be. Because of the social difficulties of epilepsy, those who suffer from the disorder and those who have some sympathy with their problems formed an association, the British Epilepsy Association, with a view to mutual help and to removal of the stigma which has always been associated with the condition. There is now a Scottish Epilepsy Association active in the formation of new branches, seeking to give club facilities for those who find themselves rejected and aiming at an extension of outlet in industry.

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country. The definitions are best taken from the Mental Deficiency Act of 1927. *Idiots* are " persons in whose case there exists mental defectiveness of

exists mental defectiveness, which though not amounting to idiocy, is yet so pronounced that they are incapable of managing themselves or their affairs, or, in the case of children in being taught to do so ". Lewis's findings for 1927 give an estimate of 52,000 imbeciles in England and Wales. *The feeble minded* are defined as being " persons in whose case there exists mental defectiveness which, though not amounting to imbecility, is yet so pronounced that they

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common. The facilities which exist for the care of such persons are, at present, quite inadequate. Many families house an imbecile or an idiot as a skeleton in the cupboard Socially, economically and emotionally this state of affairs is deplorable. There is no anguish to parents comparable to that of having a mentally defective child The presence of such a child in the family evokes the most tender and solicitous care of which the human being is capable. The

the circumstance of mental defect in a brother or sister. In Scotland the position today is that, for want of accommodation in special institutions, many defective children of the imbecile and idiot class are housed at home—a burden to every member of the family. Yet, it is the bounden duty of the State to see that ample provision is made for such cases. There is, however, another side of the problem In spite of the hopelessness of the outlook the parents,

realizes her importance if he is to survive and thinks of his dependence upon her; whereas separation of idiot from parent would be without emotional meaning to the child, it might be devastating to the parent In every case of idiocy and imbecility an attempt should be made to effect this separation, particularly when the idiot or imbecile has normal brothers and sisters As soon as the defect is recognized and the conclusion reached that institutional care is the ultimate solution to the problem, steps should be taken forthwith to see that the child is at least put on the waiting list of a certified institution for the mentally defective. What has been said about the examination of spastic children by the medical officers of Local Education Authorities applies here (see above)

The feeble minded present a problem peculiar to themselves. They are fit, under supervision, to pursue some kind of career, menial though it may be. In earlier days, more often than now, feeble minded persons were often looked after by private individuals at the expense of the Local Authority. Some were able to do labouring work in agriculture Today, the institutions for the mentally defective may farm out the less handicapped of their population. Some mentally enfeebled are defective in one particular direction in that they have no sense of morality The perpetual commission of crimes of theft and destruction, of offences with violence and of sexual impropriety, may force the segregation of the enfeebled perpetrators Thus, the authorities may be compelled to give precedence to the moderately enfeebled criminal over the

disability may be so easily imitated and appreciated One has only to shut one's eyes to realize what it must be like to live in a world of darkness No simulation can give the normal person an idea of the defects of cerebral palsy, epilepsy,

vulnerability of the eye, accounts for not a few instances of defective vision from the earliest years The rare familial disorders which prejudice vision from an early age have a low rate of survival, and are so unusual as scarcely to enter into the experience of the vast majority of the medical profession.

memory of sight can be retained and before formal education is possible; second, blindness acquired later in the period of formal education or after the individual has been established in normal social and industrial activity; *third*, blindness after a period of normal useful life has been vouchsafed, occurring

facilities are available for the congenitally blind. Special residential schools accept blind children and train and equip them for remunerative employment if they are intelligent enough to be so occupied. Responsibility for the care, training and employment of blind persons is that of the Local Authority, yet the Local Authority does not usually have facilities to deal with the whole problem. Most areas have an Outdoor Mission to the Blind and, whereas it is the duty of the Local Authority to keep a register of blind persons, their care is deputed to the local Mission for the Blind A great advance has been made in training those who have become blind after a normal youth. In Scotland the Ministry of Labour has set up a residential educational centre for the blind at Ceres in Fife where they may be trained for suitable employment.

Newly blinded adolescents and adults present a problem peculiar to themselves. Most of life has yet to be run whether or not adaptation to disability is made. Some strive to conquer the limitations imposed by darkness, others are inclined to self-pity and therefore may victimize everyone with whom they come into contact The newly blinded person in full vigour of adult life may either adjust himself to his environment or adjust his environment to himself. If the blindness has become permanent the sooner any sentimental reaction to the catastrophe is overcome, the better. Blindness, is in most instances, a permanent

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patient.

Blindness, congenital or infantile, once established as factual, need but be reported to the Local Education Authority to be dealt with. If the newly blinded person is young and has seen, has learned to read and to find his way about by sight, he has to adapt himself to an entirely new set of circumstances for which much may be done in compensation Independence and self-respect can be achieved only by substituting various acquired skills to compensate for the loss of sight. The reader must be given books to read, the musician, music to play, and the craftsman, employment worthy of his skill. Every intelligent and newly blinded young person must be taught Braille. This remarkable system is a means whereby tactile and proprioceptive sensibilities are invoked to compensate for deprivation of vision. There is no necessity to enter into any great detail about this system; it is sufficient to say that the individual symbol occupies no more than an area of $\frac{1}{8}$ inch wide and $\frac{1}{4}$ inch long. In this area all possible combinations of six elevated dots, embossed from the opposite side of a stiff paper, signify an integer or symbol to the scanning fingers. The refinements of the system have led to contraction of symbols to signify words and ... the master-pieces

The blind

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tation and has stultified learning How may the blind be diverted?—by less sometimes given free of charge, and by long-playing records of novels. the energetic blind person, the mother rearing the family, shopping and ding for them, the husband going to his business, either as administrator or erative, no measure yet has given more independent mobility than a dog ined for the purpose. In the United Kingdom, the only two centres which ain dogs for this purpose are at Exeter and Leamington.

When an adult becomes blind there are several clamant demands requiring ympathetic understanding and action. The blind person has suddenly become comparatively immobile. Adaptation to lack of mobility is slow, particularly when life has been active and the patient has indulged in much physical exertion. It is not desirable that this enforced inertia should be accepted as inevitable. Exercise in the fresh air for the blind is helpful and necessary Some member of the family or some friend should see to it that such exercise is made available. Few people know how to take a newly blinded person about One fundamental principle is to lead and not to push the blind Never take a blind person's arm, always offer the arm to the blind person Go in front, because the movements of the leader are the means of conveying to the sightless the expectation of obstacles and hazards. If the blind person has to learn Braille—this cannot be expected in the aged blind—do not read aloud too much as this tends to make the sufferer dependent on others. Braille magazines, newspapers and *Radio Times* are readily available to all and are sent at small cost There is really no reason why the intelligent, vigorous blind person cannot be wholly independent of his fellows.

The reader may wonder what the blind person can do apart from making baskets, tuning pianos, reading the Bible in public places and begging Perhaps it is not so widely known as it should be that the help the blind render to one another is greater than in any other community of disablement Many make Braille books and music scores for their fellows Again, there is practically no profession, save pictorial art, in which the blind cannot occupy a distinguished place Medicine, the Church, the Law, Teaching, Politics, have had their blind practitioners. Homer, Milton, Delius, masters of their arts though sightless, have not remained citizens of their own countries, but have, by their contribution to the common weal, become citizens of the world

Deafness.—*Congenital deafness* is very much more frequent than congenital blindness Any blind person prefers his disability to deafness Not merely is the loss of hearing a disability in itself but all that hearing can give in emotional experience, be it speech or music, is forsworn Any congenital disorder demands little or no adaptation. The central problem of congenital disorder is to find means whereby the victim may find happiness in a world very different from that of his fellows. Because of the comparative frequency of congenital deafness, there are many more schools for the deaf and dumb than for the blind Deaf persons form a social community much more readily than do the blind Gesture becomes the medium of propositional speech. The dummy alphabet has to be learned before lip-reading becomes possible The congenitally deaf has no knowledge of voice To acquire that knowledge they must be taught the various dispositions of the lips and tongue in speech and become familiar with the patterns of expired air in the utterance of the spoken word. In order to achieve this, use is made of other modes of sensation. The child is instructed to place his lips and tongue in particular positions He is made to feel the pattern of expired air in speech and to copy the mouthing of words Responsibility for

the training and education of the deaf is a compulsory obligation of the Local Education Authority. Thus, when in practice the problem arises, the child should be referred to that Authority.

Acquired Deafness.—For those who become deaf either through otosclerosis or after meningeal infection, particularly because of streptomycin therapy, an entirely different problem arises. Such people have to adapt themselves to an entirely new set of circumstances. If vision is intact and all other senses are preserved, much may be done to help the afflicted. Totally deaf people can be trained to an extent which makes their disability scarcely noticeable. In one instance at least a deaf person has attained to a distinguished career on the stage.

express himself in writing He must point out what measures are necessary to ensure that the deaf person may approach normality in the social structure. Hope of achieving normal living may avert disaster and lessen the awful depression which is certainly the lot of the newly deaf. Much can be done for those who have some degree of hearing and for whom hearing aids are of use (see p. 643).

Acquired Palsy.—In this group of disabled there are several different kinds of problem. Some palsies, traumatic or residual from infection or neoplasm, successfully treated, are permanent, static disabilities. These palsies vary in degree and extent and may not shorten expectancy of life. Another group, profoundly palsied, in a year or two may return to a state of normality with a normal expectancy of life A third class, more difficult than the first two, comprises all those who have slowly progressive palsy and have to be employed or diverted on the long downhill journey. Finally, the cause of paralysis may have dulled intellect or clouded appreciation or expression of language: this *combination of palsy and mental impairment may be static or progressive.*

Non-progressive Paralysis—Let us try to follow the course through convalescence from injury, infection or operation, to resettlement under ideal conditions During the recovery period, when it has become apparent that limitation of activity is permanent, the first auxiliary help is that of the almoner. She should interview the patient, just as soon as he is fit to give her an account of himself and his circumstances. By this means, the almoner becomes familiar with the background of home, work and leisure. Estimates of the resource of the patient and his family are made. When the time comes for the patient to face the world, the almoner is prepared to present her patient to the D.R O., who may make official arrangements for the patient under the ægis of the Ministry of Labour. Acting on her own, the almoner may interview an employer on the patient's behalf and obtain suitable work either in the patient's former place of occupation or elsewhere under sympathetic or protected conditions.

While the almoner is formulating an idea of the general position, other rehabilitative work is forging ahead. Every hospital with long-term cases has, or should have, a library. Many institutions have voluntary workers, organized among themselves, to give solace to those undergoing prolonged treatment. Funds are collected for the provision of comforts which cannot be expected from

them and the use to which their limbs are put in working a loom, doing wicker

work, painting pottery or making pictures, may be, in itself, a powerful therapeutic agent in the development of lost skills When the patient becomes more mobile the occupational therapist takes the patient from the ward to the workshop Scope for treatment is widened. The ward has ceased to be a workshop and the workshop has become a hospital Machines of particular design may be used for therapeutic ends. If, for example, a leg is palsied and recovering muscle has to be exercised, the treadle is exploited, not merely to restore function, but to produce useful articles made by the patient The psychological effect of [illegible]

which a long-term hospital can give, the patient is ready to move out He may be sent to the protected workshop or into normal industry, depending upon the residual state of disability. In the protected workshop the employee works at his own pace; the workshop exists because competition in the open labour [illegible] Fundamental [illegible] eople may keep [illegible] disabled person may be regarded by his workmates as an incubus. Transport may be an overwhelming difficulty, preventing the disabled from making the best use of their talents. Only in large centres of population is it possible for transport to be organized so that the disabled person may be employed in a protected workshop. Expense for transport should not appear as an on-cost of the protected workshop, because the deficit in industrial potential is, in itself, a big enough burden to bear. When transport to protected employment is denied, work at home should [illegible]

no opportunity should be lost in making the Local Authority aware of its duty.

For those who have severe palsy with probable recovery after a long stay [illegible]

[illegible] xes the resource of [illegible] denied; hope for recovery is lost, the charity of succour remains. Hospital and institutional care is quite inadequate and must long remain so, in a pre-occupied world. Although decline to ultimate incapacity is the lot of many, some have long periods of static disability and others perhaps of slight improvement, these periods of comparative usefulness call for very special consideration No physician can tell with certainty what to expect and therefore cannot make just provision for an unknown future. At the same time one has to recognize that the long periods of quiescence in disseminated sclerosis and amyotrophic lateral sclerosis must

be occupied with active and, if possible, remunerative employment. The Ministry of Labour is prepared to accept
from progressive disease characterized by
one must guard against over-taxing and
employment within their capacity will not harm and may help.

When occasion demands, home-help for the deteriorating paralytic is often of the greatest value. Many Local Authorities bear the expense of sending women into the homes of the disabled. This is valuable when the woman of the house is bed-ridden, perhaps incontinent, and can no longer look after her domestic affairs. Home-help is officially available until such time as the family comes home from work Such are the advantages of the home-help service in

directory gives the number and address of the Ministry of Labour Offices, the Citizen's Advice Bureau, the Social Service Organization, the Red Cross and the Women's Voluntary Service, not to mention the fact that every hospital of any size has its almoners who are able to cope with outstanding problems

Tuberculosis.—The rehabilitation and the employment of the disabled tuberculous patient are discussed on p. 123.

Heart Disease.—Problems of heart disease are no less clamant for solution. Some with adequate reserve find themselves in occupations consistent with filling a full life; at the other extreme some are home-bound and incapable of any exertion. Between these two extremes there are many to whom protected employment may come as the salvation from indolence and depression. For those who are tied by disability to the home, the almoner can usually find some work which will not overtax the impaired cardiac reserve. For those who can travel, the Red Cross treatment centre may provide diversion and productive activity at once satisfying and therefore therapeutically important. For the mobile the onus is on the Ministry of Labour to find suitable employment without arduous travel No effort should be spared to make the Ministry of Labour fully conscious of its statutory obligations in this matter. The wife and mother with a decompensated heart faces tremendous odds. For her "Home Help" should be free and readily available. At this particular point it does no harm to reiterate that Local Authorities should all have Home Help schemes. Thus, for the cardiac patient, employment should be available in open industry, in protected workshops, in modified professional practice, at diversional centres and in the home. It has always to be remembered that the metabolic expenditure created by anxiety in heart disease may exceed by far that of physical effort free from care.

These considerations of the problems of the disabled have been written against the background of the statutory and voluntary facilities as they exist in Great Britain. It is realized that in the Dominions and other countries equally pressing or special problems have to be met within a different framework and under different conditions. No matter what the extent or type of disablement may be, adjustment and employment for these unfortunate people must be

J. B. GAYLOR.

TREATMENT OF POISONING

IN PRACTICE the successful management of all cases of poisoning depends mainly on applying certain general principles which are indeed self-evident:

1. The stomach must be emptied (except in cases of corrosive poisoning).
2. Measures must be taken to combat constitutional upsets resulting from (*a*) the effect of the poison after absorption on various parts of the body, and (*b*) shock
3. Tissues damaged locally by the poison must be protected, if they are accessible, by demulcent substances.

Reference may now be made to certain practical considerations. Speed is all-important in getting rid of the poison, and while preparations are being made to wash out the stomach and to find an antidote, the following simple treatment can be given at once: if the patient is conscious, he should be made to vomit by thrusting one's fingers into his throat. This can be repeated several times after giving the patient copious draughts of water If this fails, he should be given an emetic such as a dessertspoonful of common salt or mustard stirred into a tumblerful of tepid water. Ipecacuanha and tartar emetic should not be used as they act too slowly. The same objection applies to salts of heavy metals such as zinc sulphate and copper sulphate, and these preparations cause further corrosion—especially if they fail to produce vomiting. Local stimulation of the fauces can be repeated to re-enforce the action of emetics if necessary. An alternative to reflex emetics is apomorphine hydrochloride, 6 mg ($\frac{1}{10}$ gr.). it stimulates the vomiting centre in the medulla and causes vomiting in about two minutes If it is available, there is a strong case for using it without delay, and there is a clear indication for apomorphine where the patient is hysterical or refuses to co-operate in other measures The patient is more likely to vomit if he is made to sit up after the injection, and this posture reduces the risk of inhalation of vomitus. In the fully conscious patient it is a reliable and safe drug to use, but it may fail if the patient is drowsy from narcotic poisoning, and in comatose patients apomorphine is useless because the vomiting centre is unresponsive.

Whether emetics are used or not, the stomach must be washed out. This is by far the most important part of the treatment. Unless contra-indicated by [illegible] gastric lavage should nev[illegible] stor[illegible] beer[illegible] con[illegible] administered while the stomach is being washed out. Thus, in opium and morphine [illegible] added to the water (a per-cent. or a [illegible]ing; egg[illegible] mercury) poisoning. It must be emphasized that the use of such antidotes does not compensate for delay in carrying out thorough lavage Before removing the stomach tube it is advisable to run in a pint of warm water containing two

tablespoonfuls of Epsom salts to promote evacuation of any poison which may have entered the intestine. A tablespoonful of powdered activated carbon should be added to the solution if the poison is one that can be adsorbed—such as the alkaloids and glycosides.

It is rarely possible to counteract the effects of the poison that has been absorbed. *The best that can be done is to treat symptoms as they arise.* These may vary widely at first according to the nature of the poison, but the signs of imminent danger are common to all—shock, respiratory depression and circulatory failure.

Pain may be severe in poisoning by corrosives and irritants. Morphine in full doses is indicated. The administration of tablespoonful doses of liquid paraffin hourly for the first few hours may give some relief by its demulcent action.

Dehydration is likely to occur if swallowing is painful. An adequate intake of water, salt and glucose should be provided by intravenous infusion or by rectal drip. The state of dehydration is unlikely to develop if the urinary output exceeds 1,500 ml. per day (see p. 103).

Shock should be treated by complete rest with the foot of the bed raised. Pla [illegible]

usir [illegible]
and amphetamine may be tried Their effects are fleeting, and dosage and frequency of administration are determined by the response obtained in the individual case. They are all given intravenously. Amiphenazole (Daptazole) is a new respiratory stimulant: it can be given intravenously or intramuscularly in doses of 15 mg in 1 ml. of saline.

Infection—especially pneumonia—is an important hazard. Penicillin is usually required in prophylactic or curative doses (see pp. 64, 665)

Notes on Antidotes.—(See remarks on gastric lavage above.)

POISON	ANTIDOTE
ACID (corrosive)	Magnesium oxide (magnesia): a teaspoonful moistened with cold water.
ACONITE	[illegible]
ALKALI (corrosive) .	[illegible]
ANTIMONY compounds	Tannic acid, one teaspo[illegible] water.
ARSENIC compounds .	1. Ferric hydroxide [illegible] pharmacist, while ga[illegible] 2. Dimercaprol, 3 [illegible] intramuscular injection.
ASPIRIN . . .	Sodium bicarbonate, 2 [illegible] sodium lactate [illegible]
ATROPINE and BELLADONNA.	Short-acting bar[illegible] excitement.

* *Arsenic Antidote*—The dose consists of a freshly [illegible] oxide 24 gr., triturated to a smooth paste with water, d[illegible] to strong solution of ferric chloride 85 m. diluted w[illegible] *Extra Pharmacopœia*)

POISON	ANTIDOTE
RBITURATES.	Bemigride (Megimide) is regarded as a specific antagonist. An intravenous infusion of 5 per cent glucose solution is set up, and 50 mg. bemigride in 10 ml. of saline is injected into the rubber tubing of the apparatus every five minutes until there are signs of returning consciousness.
BARIUM SALTS	Epsom salts or Glauber's salt 2 oz.
HEAVY METALS As, Bi, Hg, Au, Sb.	Dimercaprol See Arsenic above
HYDROCYANIC ACID and CYANIDES.	1 Amyl nitrite inhalations 2 Sodium nitrite solution 3 per cent, 10 ml in three minutes intravenously. 3 Sodium thiosulphate solution 50 per cent. 25 ml. intravenously
IODINE	Starch cream, or sodium bicarbonate, or magnesium oxide
LEAD SALTS	Epsom salts or Glauber's salt.
MORPHINE	Potassium permanganate (strongly *pink* solution for gastric lavage) Nalorphine hydrobromide, 10 mg intravenously, as a morphine antagonist. Dose may be repeated three times in the course of four hours if necessary Useful also in methadone poisoning.
OXALIC ACID	Magnesium oxide, chalk or lime water.
'HENOL, LYSOL and coal-tar disinfectants	Epsom salts
SILVER NITRATE	Common salt, though the gastric HCl usually suffices
STRYCHNINE	Sodium thiopentone intravenously

Poisoning by Inhalation (see also Industrial Poisoning, p. 283).—In genera practice coal gas (carbon monoxide) is the usual poison The patient must b removed at once to the fresh air · artificial respiration is then started, and th should be continued during transfer to hospital. Oxygen, or a mixture of oxyge and carbon dioxide, is usually required.

S. ALSTEAD.

1 metre is usual. The system is filled with saline solution and the delivery tube clamped. The needles are inserted through intradermal wheals of local anæsthetic solution injected in the appropriate places before beginning to assemble the drip apparatus. They may be placed (1) at the outer border of each pectoralis major muscle, directed towards the apex of the axilla, or (2) on the antero-internal aspect of each thigh, near and directed towards Poupart's ligament. Care must be taken that they do not puncture or rest in a blood vessel. When they are correctly placed, the delivery tubes are connected to them by adaptors; the needles and adaptors are then covered with sterile gauze and fixed in position by strapping. The dripper is adjusted to deliver 40 to 50 drops a minute. If 10 ml of 2 per cent. procaine solution is added to each [illegible]

tube towards the needle.

VENEPUNCTURE

Puncture of a vein may be necessary (1) for the intravenous injection of drugs or (2) for the withdrawal of blood—to obtain a sample for analysis, to obtain blood for transfusion, or to reduce the volume of blood in the circulation as a therapeutic measure. For any of these purposes, a vein in one of the antecubital fossæ is chosen. Veins may be visible and prominent, but may then slip from side to side under the skin, as if they were eluding the point of the needle. Usually the vein can be secured by stretching the overlying skin between the forefinger and thumb of the operator's free hand, but when difficulty is extreme it may be overcome by transfixing the vein from side to side with the finest hypodermic or cambric needle available so that it is immobilized; the vein is then punctured distal to the immobilizing needle. In an obese arm the antecubital veins may not be visible, but as a rule they are palpable when engorged. Care should be taken not to confuse a superficial brachial artery with a vein, particularly when intravenous medication is to be undertaken, for serious vascular complications may follow the accidental intra-arterial injection of many drugs. It is best to use one of the less movable veins situated laterally in the cubital fossa. Before a vein is punctured it should be made as prominent as possible; several manœuvres are available:

1. A [illegible]
2. The limb may be allowed to hang over the edge of the bed for a few minutes before the puncture.
3. The distal part of the limb, up to the site of puncture, may be heated by a fomentation, or by immersing it for ten minutes in hot (120° F.) water
4. (Arm). After the application of the tourniquet the patient may be directed to grasp a roller bandage firmly with his hand at intervals of thirty seconds.

In difficult cases a warm antiseptic solution (5 per cent Liquor Antisepticus) should be used for cleansing the skin ; the cooling action of spirit or ether on the skin causes the veins to contract.

Intravenou [illegible]
be employed. [illegible]
the needle, into [illegible]
needle should not be passed to the bottom of the container, but the ampoule should be tilted to allow all the fluid to be drawn up with the needle resting on the wall. [illegible]
lodge any [illegible]
the point o [illegible]
of the selected vein, and then brought over it, ready to make the puncture. When the vein is large, the position of the bevel does not matter, but when the vein is small the bevel should be held downwards, as this lessens the risk of leakage The needle is then pushed into the vein at an acute angle, and its position verified by gently[1] withdrawing a little blood into the syringe. When the point is correctly placed, the obstruction to the venous return is removed and the contents of the syringe are slowly injected. *An injection should never be made unless blood has been withdrawn into the syringe, and after this has been done the position of the needle should not be altered until the injection has been completed.* The needle is then quickly withdrawn while the thumb of the left hand makes pressure upon the area of the puncture through a gauze swab or piece of sterile cotton-wool , if the patient flexes his elbow on this pad for a few minutes, a dressing is not required

If the patient moves, there is a possibility that the needle may have been [illegible]

utilized A hot kaolin poultice, renewed hourly over the area of leakage, is the best method of reducing local irritation

To obtain a Sample for Analysis.—If possible, samples of blood for [illegible]
should be despatched to the laboratory as soon as possible after their withdrawal. A short bevelled needle of No. 19 s.w g. should be used For most single estimations amounts of 5 ml suffice ; for several different estimations 10 to 15 ml. or more are necessary. The nature of the samples required for the quantitative estimation of certain constituents of blood, and the normal range of these, are indicated in Tables III and IV When untreated blood is required, it is withdrawn into a *syringe by* venepuncture and transferred to a sterile test-tube fitted with a *rubber* stopper , the syringe must be absolutely dry to avoid any lysis of the red blood cells When an oxalated sample is necessary, blood withdrawn into a syringe is transferred to a similar test-tube containing enough potassium oxalate to cover the bottom of the tube, the test-tube being inverted, but not shaken, several times.

To obtain Blood for Transfusion.—See p 866

[1] Strong suction may draw the wall of the vein over a correctly placed needle, and so prevent the withdrawal of blood

TABLE III

Biochemical estimations, etc., for which untreated blood is required.

Constituent	*Normal Range*
Inorganic Phosphorus .	1·2–1·8 mEq./l. (3–4·5 mg.%)
Calcium . .	4·5–5·5 mEq./l. (9–11 mg.%)
Sodium . .	135–142 mEq./l. (310–325 mg.%)
Potassium . .	4·0–5·5 mEq./l. (16–22 mg.%)
Bilirubin .	0 1–0·5 mg.%
Icteric Index .	4–6 units
Acid Phosphatase	4–6 units
Alkaline Phosphatase .	6–12 units
Cephalin Cholesterol Flocculation	0–1 unit
Thymol Turbidity	1 unit
Serum Amylase	5–15 Wolgemuth units

Van den Bergh's reaction

TABLE IV

Biochemical estimations for which oxalated blood is required.

Constituent	*Normal Range*
Glucose	80–120 mg.%
Urea Nitrogen	10–15 mg.%
Non-protein Nitrogen	25–35 mg.%
Creatinine	1–2 mg.%
Uric Acid .	2–4 mg.%
Cholesterol . .	140–200 mg.%
Chlorides (as NaCl) in Plasma	101–106 mEq./l. (590–620 mg.%)
CO_2 Combining Power	25–33 mEq./l (55–75 vols.%)
Total Plasma Proteins	6·0–8 5 g.%
Albumin	3 6–5·6 g.%
Globulin	1·3–2·5 g %
Fibrinogen	0·3–0 4 g.%

Therapeutic Withdrawal of Blood.—Venepuncture has replaced venesection as a method of reducing the volume of blood in circulation; the indications for the procedure are cardiac failure with increased pressure in the systemic veins, hypertension and polycythæmia. The technique is similar to that

matching (p. 866) shows it to be completely suitable. Alternatively it may be possible to store its plasma for future use.

INTRAVENOUS INFUSION

Fluid may be introduced into a vein either through a needle or through a cannula; for the latter procedure the vein must be exposed. The chosen fluid may be given in one dose by allowing it to flow continuously, or its administration may be spread out over a period of hours or days

Apparatus.—The apparatus shown in Fig 14 is suitable for the infusion of blood or other fluids and is widely used at present in hospital practice.[1] A sterilized packet contains the attachments, which consist of a rubber bung with long air inlet tube (occluded at its outer end by a rubber cap) and short outlet tube covered by a wire gauze filter; the outlet is connected by a short piece of rubber tubing to a "dripper", from which a length of tubing (about 1 metre) leads to an attachment for needles usually of the Luer type The packet also contains a screw clamp and a test-tube holding a *needle for vein puncture*

The dripper is a glass tube into which fluid is delivered drop by drop by a narrower tube There should be a column of air between the drip tube and the level of the fluid in the main tube; if this is lost by fluid "backing up" to the drip tube, it can be restored by injecting, with aseptic precautions, a small quantity of air by means of a syringe and hypodermic needle passed through the rubber tubing immediately below the dripper.

In assembling the apparatus, it is essential to see that no part of it which is to be in contact with the fluid to be administered or with the patient's tissues should be touched by the hand, or allowed to touch anything which is not sterile

When hospital facilities are not available it may be

after its interior washed repeatedly by a stream of water; it can then be sterilized by boiling or autoclaving.

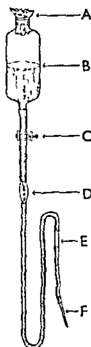


Fig. 14.—Diagram of apparatus for intravenous infusion A = sterile air-filter of cotton-wool or gauze; B = glass flask, 1 pint capacity; C = screw clip, D = glass "dripper", E = glass connection; F = record fitting and needle (or cannula).

[1] The design of intravenous equipment is at present undergoing many changes as new materials, particularly thermostable plastics, become available It is probable that within a few years disposable sets of light non-irritant plastic will be used for all intravenous therapy

Needles for intravenous infusions can be obtained in a variety of designs; they should be sharp, made of rustless material and have a short bevel. A blunt cannula, carried on a needle which punctures skin and vein[1] but is then with- [illegible] the method of insertion described below is used, straight cannulæ can and should be employed.

When the administration of intravenous fluids may have to be continued for many days (for example in hepatic failure or in preparation for the surgical treatment of pyloric stenosis) and in the restless or unconscious patient, the most satisfactory method is to thread a length of polyethylene tubing into either the superior or inferior vena cava by way of the basilic or long saphenous vein respectively. Fluid so introduced enters a large, rapidly flowing stream of blood and is immediately diluted. Solutions of a composition or concentration which would irritate the wall of a peripheral vein (e g. hypertonic glucose or saline, protein hydrolysates) can safely be administered in this manner over a period of days or weeks provided strict aseptic precautions are observed whenever the bottle connected to the infusion apparatus is changed. Immobilization of the limb is unnecessary. Lengths of polyethylene tubing for this purpose should be of size 2 or 3 (0·1 and 0 2 cm. internal bore) and can be sterilized either by boiling or by immersion in a 1 per cent. solution of cetrimide for eighteen hours.[2]

For all intravenous infusions a head of pressure of about 1 metre is ample. The container may be held in a retort stand; hung from a hook in the wall; tied to a screen, tied to a pole lashed to the head of the bed; or supported on a regular hospital type of adjustable stand. If the patient's veins are in spasm, the reservoir must be raised higher, warming the limb with a rubber hot-water bottle, electric blanket or fomentation may help to release the spasm. In extreme cases, and if very rapid infusion is desired, pressure infusion must be done by pumping air into the inlet tube of the bottle with a Higginson's syringe or sphygmomanometer bulb, and by this method up to 250 to 300 ml. of blood or other fluid may be introduced in one minute When this is done, certain additional precautions are essential: the air pumped in must be filtered through a glass connection filled with sterile cotton-wool, the rubber bung must be firmly fixed in the neck of the bottle lest it be expelled; and pressure must not be applied after the bottle is two-thirds empty because of the danger of massive air embolism.

Fluids for Intravenous Use.—These are prepared with great care from pure chemicals and distilled water, and thereafter sterilized. Unless every detail in their preparation receives scrupulous attention, pyrogenic reactions may occur In general practice it is difficult and hazardous to prepare these solutions, and the doctor is strongly recommended to procure them from firms which specialize in their production or from a hospital dispensary.

Methods of Administration.—Local complications are more prone to occur if the vein is exposed and cannulated for the administration of intravenous fluids, and therefore it is better to use the needle method for routine work.

[1] For example the Frankis Evans and West Middlesex cannulæ.

[2] The tubing must be filled with the solution, otherwise sterilization of the inner wall will be inadequate

When the veins are collapsed as in shock, or if the patient is so fat that they

wrist and elbow. If the needle or cannula is adequately secured by a turn of sterile elastic adhesive applied over a swab, it is unnecessary to splint the arm except in children or in delirious patients Veins in the lower limb should *not* be used, because satisfactory flow through them cannot be assured, especially in shock; further, the patient is immobilized by the infusion and local complications such as thrombosis are more likely

Cannula Method.—An intradermal wheal of local anæsthetic (2 per cent. procaine) is made over the vein at the selected level, about 0 5 ml of the solution is deposited in the tissues on each side of the vessel, and the area is compressed for a minute or two in order to distribute the anæsthetic A tourniquet is

passed under the vein, and the tourniquet is released. A double strand of catgut

proximal ligature is drawn to the proximal end of the cleared vein, and the first *loop of a knot is loosely tied with it Fluid is now allowed to flow through the* infusion system and cannula until all air has been displaced, when the flow is

though a good pair of manicure scissors answers very well. Care must be taken not to divide the vein completely and yet to make a large enough opening; about half the circumference of the vein is adequate. The insertion of one blade of the

placed distal to this. The cannula is best secured by passing a stitch through the skin to encircle its hilt.

Needle Method.—The vein is made prominent as already described. An intradermal wheal of local anæsthetic is made to one side of the vein at a point

should be threaded upwards along the lumen for at least 1 cm. to ensure that it is lying correctly, completely within the lumen; if this is the case, a continuous free reflux of blood will occur. As soon as blood is seen to flow from the needle

site of puncture.

Continuous Fluid Therapy—In all cases where the infusion is to be continued for a number of days care must be taken to see that fluid is accurately prescribed to meet the patient's needs and to avoid the dangers of under- or over-administration. For each twenty-four hours a careful record should be kept in which intake is charted against output. Output includes the urine, water lost

inadequate infusion.

Illustrative Case.—A middle-aged man who had begun to vomit from intestinal obstruction was admitted to hospital. During his first twenty-four hours in hospital 1,500 ml. of gastric content were withdrawn from his stomach and he did not take anything by mouth. His urinary output was 800 ml. and his insensible loss 1,000 ml., resulting in a total fluid deficit of 3·3 litres. His vomit contained virtually no sodium, potassium at a concentration of 10 mEq/l and chloride at a concentration of about 60 to 70 mEq/l. During the same period his total urinary potassium output was 60 mEq. and his urinary sodium output was 30 mEq His replacement needs were consequently 3 3 litres of water, 70 mEq of chloride, 30 mEq. of sodium and 75 mEq. of potassium. These

manner but could be disregarded.

The period during which an infusion into a vein may be continued varies ... is administered; ... heat-sterilization, ... further probable factor producing inflammation of the intima of the vein is an unknown substance present in rubber tubing which is gradually washed out by the fluid being administered. With conventional methods of administration by needle or cannula the vein sooner or later becomes the site of a non-infective phlebitis, ushered in by a feeling of local soreness; later the tissues in the immediate

The development of phlebitis can largely be prevented by changing the site of infusion at intervals of not more than thirty-six hours, by the use of plastic infusion sets, and, as has been mentioned, by the use of polyethylene cannulæ discharging into a vena cava.

BLOOD TRANSFUSION

Blood is collected from a donor by mixing it with a suitable anticoagulant; it may be infused immediately into a patient or it may be stored in hermetically sealed bottles in a refrigerator until required.[1] Whether fresh or stored blood is used, certain precautions must be taken to ensure that the transfusion is without danger to the patient

General Precautions.—The person from whom the blood is taken must be physically healthy; more particularly there should be no history or present evidence of any disease transmissible by blood (e g malaria, infective hepatitis, syphilis, etc). The Wassermann reaction of a donor's blood should be proved to be negative.

At all times the blood must be protected by the most rigid aseptic technique rom contamination by organisms The sterilization of apparatus should be *y heat* (because antiseptics may spoil the blood), but the apparatus must not be hot when used and the blood must never be warmed above 40° C. (104° F.) because of the danger of denaturing its proteins For storage the temperature should be about 4° C (the temperature of a domestic refrigerator) and should never be as low as 0° C., at which the cells are damaged Blood removed from storage should be used within six hours and should be free from hæmolysis—indicated by a red discolouration of the zone of plasma above the cell layer. Finally, blood must never be infused until it has been proved by suitable tests to be compatible with the blood of the patient.

Blood Groups and Compatibilities.[2]—Many different blood groups have been distinguished and the number is steadily increasing, but transfusion practice is concerned mainly with the four chief groups (AB, A, B and O) and with the Rhesus factor. The four groups are so named because of the presence or absence of two agglutinogens named " A " and " B " in the red cells Corresponding to these agglutinogens are their homologous antibodies or agglutinins named " Anti A " and " Anti B " respectively The agglutinin is present in the serum of any blood from whose cells the corresponding agglutinogen is absent. This reciprocal arrangement is shown in Table V

It will be seen that when any two whole bloods of different groups are mixed, some incompatibility will result the red cells of at least one of the two bloods will contain an agglutinogen which corresponds to an agglutinin in the serum. Thus mixture of two whole blood samples will result in some agglutination unless the bloods are of the same group In giving blood transfusions, it has been found that in routine practice the effect of the serum of the donor on the red cells of the recipient can be almost completely neglected, only the effect of

[1] Blood so stored is not transfused after twenty-one days because by this time not only are the cells more prone to undergo lysis but also the potassium concentration in the plasma has risen to dangerous levels by release of this substance from the cells

[2] For a full description of the blood groups and for a valuable account of modern transfusion practice see M R.C. War Memorandum No 9, " The Determination of Blood Groups ", and M.R.C. Memorandum No 27, " The Rh Blood Groups and their Clinical Effects" H M Stationery Office.

the serum of the recipient on the corpuscles of the donor need be considered This means that the blood infused does not always require to be of the same group as that of the patient : it must, however, be of a group whose cells will

TABLE V

Blood Group (and Agglutinogen in Cells)	*Agglutinin in Serum*
AB	None
A	Anti-B
B	Anti-A
O	Anti-A and Anti-B

not be agglutinated by the serum of the patient. Reference to the table will accordingly show that :

The Rhesus or Rh factors [1] are a group of antigens present in the red cells of about 85 per cent. of human beings. The remaining 15 per cent. are Rh-negative. In certain circumstances Rh-negative individuals may develop in the [illegible] "Rh-positive". Th[illegible] blood or [illegible] fœtus, the [illegible] egative woman is made Rh-sensitive either by transfusion or by her first pregnancy, any Rh positive fœtus which she subsequently conceives is affected by the Rh antibodies ; in consequence the fœtus may be still-born or it may be born with hæmolytic anæmia and the condition of erythroblastosis fœtalis In the circumstances mentioned above, both mother and child must be regarded as " Rh-sensitive ", and if they are to be transfused, Rh-negative blood must be used Similarly, if repeated transfusions are undertaken in Rh-negative patients, sensitization occurs unless Rh-negative blood alone is used, and a subsequent transfusion of Rh-positive blood will result in a reaction with hæmolysis of the donor's cells

In practice, transfusion of Rh-positive blood to an Rh-negative patient must be avoided except when the urgency is such that life can be saved only by accepting the risk. Particular care must be taken to ensure that Rh sensitivity is not produced in any female child or any woman in the child-bearing period and that Rh-positive blood is not given to a patient who may have previously been sensitized to the Rh factor. The possibility of such Rh sensitivity must always be considered in a person who has received previous blood transfusions or in any parous woman

Stocks of Group O Rh-negative blood are maintained by Blood Transfusion

[1] The name Rhesus is used because these antigens were first detected by the use of anti-Rhesus serum prepared by injecting the red cells of the Rhesus monkey into rabbits

Centres for use in emergencies when the administration of blood must precede the determination of group and Rhesus type. However, supplies are limited and its use is not justifiable unless it is proved to be necessary. Fortunately the rapid

[illegible]

groups giving rise to incompatibility between the bloods of donor and patient is avoided by a direct test of compatibility. All generalizations on the A.B.O. or

[illegible]

omission of a direct test is not justifiable except in circumstances of extreme [illegible] war;

[illegible] ability rests upon the practitioner undertaking the grouping and compatibility testing of blood for transfusion, and it is necessary to adopt a technique devoid of the risks of clerical or technical error

Blood Transfusion Centres carry out all procedures in test-tubes 5 cm. by

[illegible]

to Table V will show that the group of any given blood can be determined by testing its corpuscles separately against two sera, one of which contains only

[illegible]

agglutinin required is best preserved by storing the serum in the frozen state in [illegible] Because it is suitable for emergency use

[illegible]

added to a drop of Anti-A serum and to a drop of Anti-B serum placed at opposite ends of a glass slide appropriately marked. each suspension is stirred with a separate clean glass rod or a new wooden match to ensure that there is no transference of agglutinins from one part of the slide to the other. The

slide is either carefully marked on its under surface with a grease-pencil or placed in a special rack marked "Anti-A" and "Anti-B" at either end. If agglutination is going to occur, as a rule it does so rapidly, but an interval of fifteen minutes should elapse before the results are finally read. During this time evaporation should be prevented by placing the slides on damp filter paper and covering them by inverted glass dishes. Agglutination is usually obvious to the naked eye, but in all cases the cells should be scrutinized under the low power of the microscope. According to the findings, the blood group of the person being tested can be determined thus:

TABLE VI

Agglutination of unknown Cells by		*Unknown belongs to*
Anti-B Sera	*Anti-A Sera*	
+	+	Group AB
–	+	Group A
+	–	Group B
–	–	Group O

The Rhesus group can be determined at the same time. One drop of the

patient is Rh-positive.

Finally, the group of the unknown blood may be checked by testing its serum against known cells. Serum is obtained by centrifuging the sample of blood; one drop is added to a drop of Group A cells and a separate drop of Group B cells placed at the ends of a slide. The slide is examined after ten minutes both by the naked eye and under the microscope. The serum test is read as follows:

TABLE VII

Unknown Agglutinates		*Unknown belongs to*
Group A Cells	*Group B Cells*	
+	+	Group O
–	+	Group A
+	–	Group B
–	–	Group AB

[1] In certain circumstances the facilities for these procedures may not be available. The tube should then be placed in warm water at the temperature of the practitioner's hand, and after fifteen minutes, read directly under the microscope without attempting to observe the sediment.

Technique for Emergency Blood Grouping and Compatibility Test

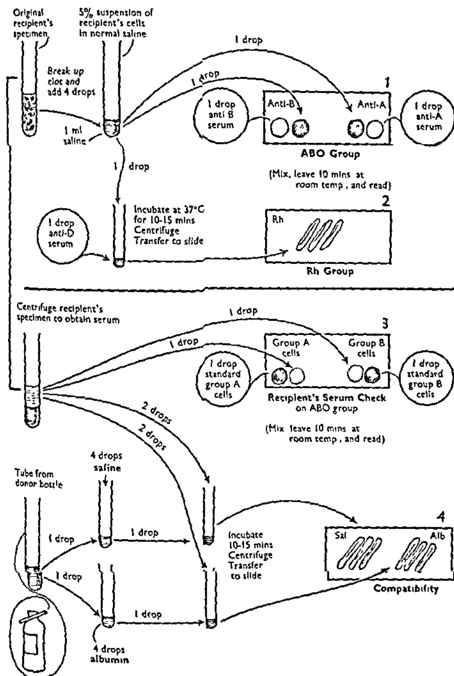


Fig 15

With acknowledgments to Dr R A Cumming, Director of South-East Scotland Blood Transfusion Centre

Direct Test of Compatibility.—The direct test of compatibility must be made between the cells of the donor and the serum of the recipient. In addition, some of the Rh antigens in the serum of the recipient can be detected only if the cells of the donor are suspended in human albumin, and this is now an essential part of an adequate compatibility test. The compatibility test should be carried out as follows:

Two suspensions of cells from the donor are made by mixing one drop of blood obtained by finger prick with four drops of saline, and another drop of blood with four drops of 20 per cent. human serum albumin. If stored blood is to be used, cells for this test are usually provided in a small test-tube (known as the pilot tube) attached to the blood bottle.

[illegible]

sealed at both ends in a flame and the serum given time to separate or obtained by centrifuging.[1]

Two drops of the recipient's serum are then mixed in test-tubes with one drop each of the saline and albumin suspensions of the donor's cells. These tubes are then incubated for ten to fifteen minutes at 37° C. and centrifuged for twenty seconds. The sediment is transferred to a slide and examined under the microscope. If the blood is compatible, agglutination should not take place with either the saline- or albumin-suspended cells of the donor.

[illegible]

Rhesus factor and for establishing direct compatibility between donor and recipient are the simplest available and should be used in an emergency only. Whenever possible the blood of the recipient should be submitted to a Transfusion Centre where more complex tests can be applied and the possibility excluded of rare incompatibilities not revealed by the simple tests The emergency methods available to the practitioner are summarized in Fig. 15, which demonstrates a continuous technique for grouping and direct matching which can be carried through in the minimum of time with the maximum of safety

Collection of Blood for Transfusion.—When the indications are for the transfusion of *fresh blood* or in an emergency when blood is not available from a Transfusion Centre, the practitioner may have to select a suitable donor and withdraw the blood himself. The principle of the method does not differ from that used in Transfusion Centres, but the apparatus may have to be improvised.

[illegible] already described

available, the direct compatibility test must suffice

Technique—The donor should be recumbent. The cuff of a sphygmomano- [illegible] the [illegible] ound [illegible] three

[1] A centrifuge may be improvised by fastening the tube by sticking plaster to a blade of the fan of a motor-car or to the "rim end" of a spoke of the back wheel of an upturned bicycle.

drops of local anæsthetic are injected into the skin over the vein at the site to be

vein consists of a needle of wide

75 cm.) rubber tubing, the whole

he blood is received into a sterile jar or bottle; the receptacle contains sterile (3 8 per cent) sodium citrate solution as anticoagulant. This solution must be prepared from pure salt and freshly distilled water, the solution being sterilized by boiling or in the autoclave; alternatively, a sterile concentrated solution may be purchased,[2] and diluted with sterile distilled (pyrogen-free) water For each 90 ml. of blood to be transfused, 10 ml of 3 8 per cent citrate solution are required; it is convenient to start with 50 ml. of the citrate solution in the receiver and to withdraw about 450 ml. of blood. Before the needle is inserted into the vein, needle and tubing should be washed through with sterile citrate solution. The vein is punctured and

collected, first the tourniquet is released and then the needle is withdrawn. The puncture is covered with a sterile pad of gauze, and the arm is firmly bandaged. The removal of 450 ml. of blood from a healthy adult is seldom attended by any unpleasant effects, but it is advisable to keep the donor recumbent for fifteen to twenty minutes after completing the withdrawal.

Administration of Blood.—*Fresh Blood*—If the apparatus described is available (see Fig 16), it should be used for the administration of fresh blood If the blood has been collected into an open receptacle, it must be

with stored blood. It is, however, a wise precaution to pour the blood into the reservoir through three or four layers of sterilized gauze

Stored Blood.—The Blood Transfusion Centres collect blood from suitably selected donors of known blood group This blood is prevented from coagulating by mixture with a solution containing sodium citrate and preserved by the addition of dextrose, and is stored in refrigerators until required It can generally be used with safety up to three weeks from the date of withdrawal

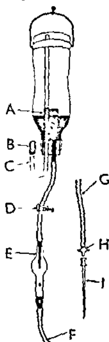


FIG 16.—Diagram of apparatus for blood transfusion: standard type supplied by blood transfusion services A = wire gauze filter, B = rubber cap (sometimes with glass rod) to occlude C = inlet tube; D = screw clip to control rate of flow, E = glass "dripper"; F and G = rubber tubing about 3 ft. long; H = record type fitting for I = needle or metal cannula.

1 g of sodium citrate in 4 ml

50 ml with distilled water, are

shown on the label on the blood bottle, but the older the blood when it is used, the less lasting will be the benefit to the patient. The corpuscles of blood which has been stored for more than a few days will survive in the circulation of the recipient for a relatively shorter time, and though such blood will be entirely serviceable for the treatment of shock due to hæmorrhage, it will be less useful in the treatment of chronic anæmia.

... sealed by a
scre ... containing a
quai ... tibility tests
(p. 866).

The blood should be inspected for evidence of hæmolysis in the supernatant plasma.

Apparatus of the type described on p 867 is used for the administration of blood. If it is to be administered rapidly, it is desirable to warm it slightly. Standing at room temperature for an hour or two will be sufficient, or the bottle can be immersed in warm water for fifteen to twenty minutes This water should never be warmer than 40° C., a temperature which the practitioner's hand can bear with complete comfort. The blood should be mixed only by gentle inversion of the bottle once or twice before the screw cap is removed.

Infusion of Concentrated Red Cells —The infusion of concentrated red cells raises the hæmoglobin level with minimal addition to blood volume, and it is therefore of value in the rapid correction of anæmia. Fresh blood not more than a week old is used, the supernatant plasma and white cells being withdrawn ... The contents of the two bottles of ... Concentrated red cells should not ... " as they deteriorate rapidly. ... ransfusion Centres prepare and provide bottles of blood plasma.[1] It may be supplied in liquid form and with pre-sterilized apparatus, exactly as for blood transfusion. Liquid plasma should be an absolutely clear solution and *must* be discarded if it shows any opacity or opalescence Sometimes it is dried[2] and supplied in the form of a yellow powder · *it must then be reconstituted for administration by the addition of* sterile distilled water The quantity of distilled water which must be added is ... he bottle, about 400 ml is required for 30 g. ... *used for reconstitution must be pyrogen-free* ... venous administration To effect complete solution, the bottle must be shaken for about five minutes and the reconstituted plasma *should be used at once.* The plasma solution produced in this manner is usually opaque from the presence of lipoid particles; nevertheless, it is safe to give it intravenously. Plasma is used in cases of shock or of hæmorrhage when whole blood is not immediately available; it is particularly indicated in severe burns and crush injury in which plasma is the predominant fluid lost and in which hæmoconcentration is a feature. Tests of compatibility are not required.

Reactions to Transfusion of Blood or Plasma.—Minor reactions may occur during transfusion—usually shivering followed by fever and headache or

[1] Some Transfusion Centres also supply serum on request Serum is used in the same way as plasma and has no particular advantage.

[2] Dried plasma or serum can be safely stored for several years under any condition of temperature Wet plasma can, however, be kept at room temperature for long periods, and it is probable that if it is stored in this manner for six months before use the risk of homologous serum jaundice is reduced

the rate of delivery should be reduced to fifteen or twenty drops a minute: if

dyspnœa and circulatory collapse Its nature is recognized from the development of an urticarial rash, which may be widespread Such reactions are most likely to occur if the same donor is used for a second transfusion to the same recipient. Though alarming, they are seldom serious, but if recognized while the transfusion is in progress, the flow should be stopped Adrenaline, 0·5 ml. of 1 : 1,000 solution, is given subcutaneously and followed by 15 mg. of morphine sulphate. If urticaria persists, one of the antihistamine drugs should be given by mouth

Rarely, minor reactions occurring after completion of a transfusion are due

Severe reactions are due to mistakes in cross-matching resulting in the rapid agglutination and hæmolysis of the transfused red cells. Soon after the transfusion is begun, the patient becomes restless and complains of lumbar pain or

circulatory collapse is severe in the early stages, it should be combated by transfusion of compatible blood, of plasma or of a plasma substitute. All urine passed by the patient should be measured and a record kept of fluid intake and output. If signs of renal failure appear, the treatment is as described on p 714.

[1] The rubber tubing and other attachments which are used for transfusions are meticulously

cleft (Fig. 19), or into the muscle mass on the lateral aspect of the thigh. When a series of intramuscular injections are to be given, the site should be varied by [illegible]

and steadied by the forefinger and thumb of the left hand; the needle is held in the forefinger and thumb of the right hand, and is plunged through the skin [illegible]

slowly and steadily completed and the needle withdrawn. Thereafter the area is massaged firmly for a minute or two, to ensure even dispersion of the injected material.

PARACENTESIS OF THE ABDOMEN

This is indicated for diagnostic purposes and when ascites embarrasses movement, respiration or the action of the heart. [illegible]

catheter. If the abdomen is hairy, it is shaved. The patient should be in a semi-reclining position, so that the fluid gravitates towards, and the intestines away from, the lower abdomen; and before the abdomen is tapped a broad binder (or roller towel) should be placed round the upper part of the abdomen. This is tightened as the fluid escapes, and thus faintness from reduction of intra-abdominal pressure is prevented. Either of two methods may be employed for the withdrawal of fluid: a trocar and cannula may be used in order to drain the abdomen rapidly; or the ascitic fluid allowed to run continuously for twenty-four to thirty-six hours through a fine rubber or polyethylene tube.

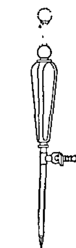


Fig. 18.—Trocar and cannula for paracentesis of the abdomen.

(By courtesy of Down Bros., Ltd., London.)

By Trocar and Cannula.—An ordinary trocar and cannula with a bore of about 12 s.w.g. is adequate. A scalpel with a narrow blade is required, and a length of rubber tubing selected just wide enough to attach to the end of the cannula and long enough to reach a receptacle at the side of the bed. The abdomen is cleansed and sterile towels are placed around the selected point. An intradermal wheal is raised here with procaine solution. The deeper tissues are also infiltrated, but it should be remembered that the stretched abdominal wall of the ascitic patient is usually very thin and only shallow infiltration is required. A small cut is made through the skin, of such a size that it will admit the point of the trocar and stretch to accommodate the cannula. The cannula with trocar in position is then pushed slowly through the abdominal wall; while doing this the right forefinger is kept firmly upon it to guard against its plunging too far into

of bowel floats up and obstructs the cannula so that the flow ceases. It can be restarted by moving the cannula up and down or from side to side. Occasionally a flake of lymph blocks the cannula; this can be dislodged by the cautious reinsertion of the trocar. As the abdominal swelling decreases the binder is tightened; but if the patient complains of faintness the flow is temporarily ... ases, the cannula is with-

... on of fluid is large and gradual drainage is required, the most convenient method is to puncture the abdominal wall with a trocar and cannula, as already described, and to thread 4 to 5 cm. of fine rubber or 2 mm polyethylene tubing along the cannula into the peritoneal cavity. The cannula is then withdrawn and the tube connected to the receptacle at the bedside Often the flow of fluid will begin at once; if it fails to do so, a syringe may be attached to the external end of the tube and gentle suction applied in order to establish syphon action.

ASPIRATION OF THE PLEURAL CAVITY

This may be necessary either as a diagnostic procedure to determine the physical, cytological and bacteriological nature of a pleural effusion, or as a therapeutic procedure to withdraw from the cavity a considerable amount of liquid (for example pus in empyema, effusion in cardiac failure or blood in hæmothorax).

Although it is occasionally necessary to choose an interspace which lies directly over the site of the effusion, as determined by clinical and especially radiological evidence, as a rule the puncture is made in the eighth intercostal space, in the posterior axillary line, and nearer the ninth than the eighth rib in ...

procaine solution at the point selected for puncture and 2 ml of the solution is then infiltrated into the tissues of the chest wall It is essential to wait a few minutes to give the anæsthetic time to act and to reach the pleura

Removal of a Sample.—A wide-bore (14 to 16 s w g) short-bevelled needle is attached to a 5 ml. syringe and the needle is inserted through the wheal of local anæsthetic into the pleural cavity. Negative pressure is main- ...

with a sterile swab.

Aspiration as a Part of Treatment.—A large syringe (50 ml) is used This is connected to the aspirating needle by 12 cm of stout rubber tubing. The aspirating needle is passed into the cavity as described and the syringe ...

into the pleural cavity should be avoided because pneumothorax induced accidentally is not invariably free from complications. Aspiration is continued

sediment in a series of specimens.

If the aspirated fluid is to be replaced by air, this should be done gradually: after the syringe is emptied it is filled with a slightly smaller quantity of air, which is introduced slowly into the pleural cavity. An alternative method is to insert the needle of an artificial pneumothorax machine through a separate puncture in the chest wall and to adjust the pressures so that air equal in volume to that of the liquid withdrawn is gradually introduced. The introduction of air in this manner prevents sudden mediastinal shift.

Penicillin may be introduced into the pleural cavity after aspiration has been completed. A clean syringe is charged with an aqueous solution of crystalline

confirmed that the

e is replaced by the

re of the pleura is immediately followed by pleural shock, a condition characterized by extreme cardiac and respiratory failure. It is probably due to air embolism, and if it occurs the needle must be withdrawn immediately. The treatment includes warmth, artificial respiration if necessary and the intravenous injection of 2 ml. or more of nikethamide.

PARACENTESIS OF THE PERICARDIUM

The skin is cleansed and sterilized and then anæsthetized by intradermal

site of puncture. The following sites are usually employed: (1) in the interspace, outside the apex beat but inside the limit of cardiac dullness; (2) in the fourth left interspace about 3 cm. from the sternal margin (far enough from the bone to avoid the internal mammary artery which descends in this region), ... and the lowest ribs *the needle*

, (4) from

seventh or

eighth intercostal space Of these, the first two are those most generally used and appear to be devoid of risk The penetration of the heart muscle by the needle is of no consequence provided that large coronary vessels are not punctured; this is an unlikely accident from a needle inserted outside the apex

beat or over that part of the right ventricle which lies 3 cm to the left of the sternum—a zone of the myocardium in which there are few large vessels The epigastric and posterior routes are occasionally preferable when a loculated effusion has to be reached; the fluid is reached at a lower level than when an anterior puncture is performed, and therefore more complete drainage can be carried out When large quantities of fluid are being removed, the rate of withdrawal should be slow, to avoid the risk of dangerous pressure changes in the pericardium and the heart.

LUMBAR PUNCTURE

This consists in the introduction of a hollow needle into the subarachnoid space in the lumbar region, a procedure which is employed for both diagnostic and therapeutic purposes. A lumbar puncture needle must be of fine bore, with a sharp, shortly bevelled point and a closely fitting stilette It is so marked that the line of the bevel can be checked by examining a mark on the base of the needle Occasionally a needle of large bore is needed to withdraw thick exudate, but even "thick" liquids (such as lipiodol) can be introduced through a fine needle if the ampoule containing the liquid is warmed in a bowl of hot sterile water to a temperature of 110° F and the barrel of the syringe is kept warm by covering it repeatedly with gauze swabs soaked in the hot water

Technique.—In most cases the puncture must be performed with the patient in bed, but if his surroundings or size permit, it is more easily carried out as he lies on a firm surface, such as a kitchen table or operating table He should lie on his left side, and a small pillow is placed under his head in order to keep the cranial and spinal parts of the subarachnoid space at the same level The patient then bends his head slightly forwards and clasps his knees with his hands, so as to arch his back and thus open out the spaces between the spinous processes of the lumbar vertebræ (Fig 19) Only in the most unruly or unco-operative of adults is an anæsthetic needed, and usually a child can be gently but firmly held in the same position Inhalation anæsthesia interferes with the accurate measurement of cerebrospinal fluid pressure, and if this information is important, morphine and hyoscine or pethidine should be tried first for an adult and chloral hydrate for a child.

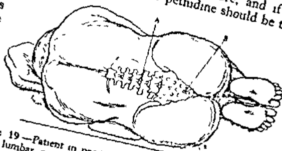


Fig 19—Patient in position for lumbar puncture A, Site for lumbar puncture, B, Site for epidural injection The stippled areas are suitable for intramuscular injections

Usually the needle is inserted between the spines of the third and fourth lumbar vertebræ, a level which corresponds to the point where a line joining the highest points of the iliac crests crosses the spinal column. After the usual skin preparation, and with a towel in position, this point is identified with the left thumb and a wheal is raised by intradermal injection of local anæsthetic in the midline with a fine hypodermic needle A longer needle is used to infiltrate the deeper tissues in a forward and slightly cranial direction; *the needle*

should never be sunk to its full extent

from the surface which varies with age and build (in the average adult, 4 to 5 cm.) the needle is felt to overcome a certain resistance—that of the ligamentum subflavum between the laminæ. If it is pushed onwards for 0 5 cm. it will have pierced the dura and entered the spinal subarachnoid space.

Difficulties in Lumbar Puncture.—Lack of co-operation on the part of the adult patient should be met with only in those who are mentally confused or delirious; and even in these circumstances firm holding, careful local anæsthesia and patience will enable the puncture to be completed in the majority of cases. As a rule the same plan is successful in children. If the bed is soft, allowance must be made for the tilt of the patient's body, the needle being directed a little downwards as well as forwards and cranially. When the needle impinges on bone before entering the spinal canal, it is usually found to have been pushed in too caudal a direction; it must be withdrawn for 3 cm. before being advanced more cranially If there is gross spondylosis, great patience may be required in searching for a gap between the laminæ; another lumbar interspinous space may have to be explored—for example, between the second and third spinous processes. If the fluid which drops from the needle is blood-stained, a little should be allowed to run down the wall of a test-tube held on a background of white gauze. If the tint becomes progressively less deep, it is likely that a small vessel has been opened by the needle, and readings of cerebrospinal fluid pressure may be taken. Later two or three samples are collected in a series of tubes, and those that are clear (or less deeply tinted) used for investigation. When the cerebrospinal fluid already contains blood, the tinting persists and may be assumed to be of diagnostic importance. The significance of

procedure It is estimated in terms of millimetres of cerebrospinal fluid, and the reading must of course be made before a sample is taken. The needle is connected by means of a three-way stopcock and adaptor and a short length of rubber tubing to a manometer made of glass and graduated in centimetres; the whole apparatus must be sterilized by autoclaving or boiling, but it should be remembered that pressures taken using a wet manometer may be inaccurate. The stopcock allows the operator (1) to close the lumen of the needle, (2) to allow

less unless the patient is relaxed and breathing quietly; and these requirements may be secured only by waiting and by reassuring the patient. Normally the fluid shows oscillations up to 0.5 cm. with each beat of the pulse and up to 1 cm. with each respiration; the mean is taken as the initial pressure.

If the subarachnoid space above the level of the needle is free from obstruction, variations in cerebrospinal fluid pressure will be indicated in the manometric levels. Rhythmic fluctuations of pressure with the arterial pulse and respiration are evidence of free communication. The situation may be investigated further by the manœuvre of Queckenstedt. Normally the compression of both internal jugular veins by an assistant for four seconds (the patient having been previously warned) leads to an increase in pressure in the intracranial veins of anything up to 30 cm. of water. If there is no obstruction to the free flow of cerebrospinal fluid, such venous compression is accompanied by a prompt rise in the level in the manometer, and the manometric pressure falls abruptly when the jugular compression is released. If obstruction of the subarachnoid space is present, for example by a spinal tumour, then when jugular com-

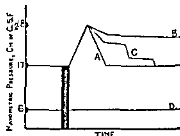


FIG. 20.—Diagrammatic representation of manometric response to jugular pressure. The black block represents compression of the internal jugular veins for four seconds. A, normal response, B, new higher level, C, "stairway," fall, and D, lack of response (complete block).

TABLE VIII

Condition	Pressure Mm.	Colour	Coagulum	Cells. Per Cu. Mm.	Protein Per Cent	Glucose Per Cent	Chlorides. Per Cent	Wassermann
Normal	80 to 175	Clear	None	0 to 3 (L.)	0.015 to 0.025	0.04 to 0.08	0.72 to 0.73	Neg
Acute meningitis	+ + +, to 1 000	Turbid to purulent	Present	+ + + (P.)	0.5 +	Dim. or absent	Nor. to 0.6	"
Tuberculous meningitis	+ +	Clear to turbid	Us. (fine)	+ + (L.), occas. + (P.)	0.05 to 0.5	"	Nor. to 0.55	"
Acute syphilitic meningitis	Us. + to + +	"	Occas. (fine)	"	0.04 to 0.4	Us. nor.	V. slt. dim.	Pos., 85%
Vascular neurosyphilis	Nor. to +	Clear	None	Nor. to + (L.)	0.15 to 0.5	Nor.	Nor.	" 75%
Tabes dorsalis	Nor.	"	"	Nor. to 200 (L.)	Nor. to 0.1	"	"	" 80%
Dementia paralytica	Nor. to +	"	Occas. (fine)		0.25 to 0.5	"	"	" 100%
Benign lymphocytic meningitis	"	"	Rare	25 to 500 + (L.)	0.02 to 0.07	"	"	Neg.
Acute anterior poliomyelitis	"	"	Occas. (fine)	+ + P., later + L.	0.02 to 0.35	"	"	"
Epidemic encephalitis	Us. nor., rarely +	"	None	10 to 500 (L.)	Nor. to 0.08	"	"	"
Disseminated sclerosis	Nor.		"	Us. nor., rarely + (L.)	Nor., or + (0.15)	"	"	"
Polyneuritis ("neuronitis")	Nor. to +	"	"	Nor. to +	Us. + to 0.75	"	Nor. to dim.	"
Aseptic meningeal reactions	Us. + to + +	Clear to turbid	Occas.	To 10 000 (P.)	0.07 to 0.2	"	"	"
Cerebral abscess	"	Clear to purulent	"	+ to 800 (P., L.)	+ to 0.2	Nor. occas. dim.	Nor.	"
Supratentorial cerebral tumour	"	Clear occas. yellow	None	Nor. to 150 (L.)	Nor. to 2.0	Nor.	"	"
Infratentorial cerebral tumour	"	"	"	"	Nor. to 0.5	"	"	"
Spinal cord tumour	Low (Block)	Clear to yellow	Occas.	Nor., occas. +	0.04 to 3.5	"	"	"
Spontaneous subarachnoid haemorrhage	Us. + +	bloody xanthochromic	None	+ +, R.B.C.	0.02 to 1.0	Nor., occas. dim.	"	"

dim.=diminished. L.=Lymphocyte. nor.=normal. P.=Polymorph. us.=usually.

[illegible]

pressure is applied or released (partial block)

When block is present, the *initial pressure* is low ; but manual compression of the abdomen will be followed by a rise in pressure, even when response to jugular compression is absent.

[illegible] the [illegible]

fluid is allowed to drip slowly into a tube or a series of tubes for further examination. Tubes should be sterile and chemically clean, and should be fitted with rubber stoppers Fifteen millilitres of fluid is sufficient for all routine analyses, but when a space-occupying intracranial lesion is present or is suspected, the withdrawal of fluid should be restricted to an amount which does not reduce the manometric pressure by more than one-third of the initial reading.

The only absolute *contra-indication* to lumbar puncture is that the diagnosis has already been firmly established . in these circumstances the procedure is superfluous. Lumbar puncture is not a major or dangerous procedure, but, on the other hand, a casual attitude towards the technique is reprehensible and the procedure should not be allowed to become routine. Relative contra-indications are the circumstances in which the chance of infection is high, such as in unsuitable surroundings, or when the patient's back is repeatedly soiled by fæcal or urinary incontinence.

The number of tubes into which the sample is received depends upon the type and number of tests which are desired and on the requirements of the laboratory or laboratories to which samples are to be sent. Thus, information may be desired on the (1) chemical, (2) cytological, (3) bacteriological and (4) immunological properties of the fluid (Table VIII). Three separate samples usually satisfy the most exacting of laboratory colleagues.

After the needle has been withdrawn, the skin puncture should be covered with a small dressing held in place by adhesive. The patient should be kept in the recumbent position for twenty-four hours in order to avoid the unpleasant sequel of " lumbar puncture headache ".

[illegible] needle break off under [illegible]

CISTERNAL PUNCTURE

For diagnostic or therapeutic purposes the cisterna magna of the subarachnoid space may be tapped through the atlanto-occipital ligament. This procedure has the advantage over lumbar puncture that it is not attended by the [illegible]

canal It is potentially more dangerous than lumbar puncture because of the proximity [illegible]

Techni[illegible]

[illegible] crosses the spine. The skin is anæsthetized by intradermal infiltration of local anæsthetic. [illegible]

[illegible] forwards through the atlanto-occipital membrane and dura (which are felt to "give") into the cisterna magna, normally in an adult this lies at a depth of 4 to 6 cm from the skin. When the needle is disconnected, fluid drops slowly or may [illegible]

[illegible] thumb and fingers of the left hand When the needle is withdrawn, the puncture is sealed with adhesive.

ASPIRATION OF JOINTS

Methods of puncturing the cavities of joints for diagnostic and therapeutic purposes are shown in the diagrams and described in their accompanying legends.

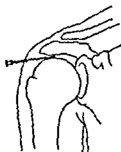


Fig 21 —*Shoulder joint* From immediately distal and somewhat posterior to the tip of the acromion process, the needle passes medially and a little cranially, over the humeral head

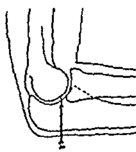


Fig. 22.—*Elbow joint* With the forearm at right angles, and midway between pronation and supination, the needle passes anteriorly from a point immediately proximal to the head of the radius

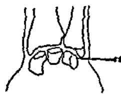


Fig. 23.—*Wrist joint.* From a point immediately distal to the styloid process of the ulna, the needle passes laterally.

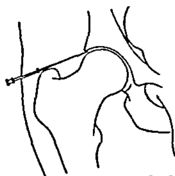


FIG. 24.—*Hip joint.* From a point immediately proximal to the mid-point of the upper border of the greater trochanter, the needle passes medially and slightly cranially, along the neck of the femur.

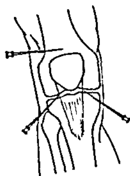


FIG. 25.—*Knee joint.* The needle may pass from either the medial or the lateral side (1) into the suprapatellar pouch, or (2) into the joint on either side of the ligamentum patellæ.



FIG. 26.—*Ankle joint.* From a point immediately distal to the tip of either malleolus, the needle passes cranially, and towards the median line of the tibia, between the malleolus and the talus.

JAMES LEARMONTH.
H. A. F. DUDLEY.

OXYGEN THERAPY

Oxygen supplied for medical use is specially prepared so as to be free toxic constituents. Cylinders are available both of pure oxygen and of oxyg containing from 5 to 10 per cent. of carbon dioxide. These carbon dioxi oxygen mixtures were introduced in the belief that it was sometimes advantage to stimulate respiration by increasing the carbon dioxide content of the alve air, but it is now considered that such stimulation is seldom either necessar desirable. In some patients the addition of carbon dioxide may stim respiration so violently as to cause severe distress Others, whose respir centres are depressed by anoxia or by drugs, or whose lungs are grossly dise may be unable to increase their pulmonary ventilation sufficiently in res to the inhalation of carbon dioxide to keep the tension of this gas i blood within normal limits If its administration is continued in such respiratory acidosis will develop.

In most hospitals there are adequate facilities for the supply of o In an increasing number pipe-lines from a central bank of cylinder oxygen to the operating theatres and to individual beds in the wards. I hospitals, however, the position is still unsatisfactory. Problems are, of most likely to arise in those without a piped oxygen supply. The cylinders may be too small to cover emergency requirements, or a su careful check may not be kept on their content of oxygen with t that only empty or half-empty cylinders are available for the treatm seriously anoxic patient.

When individual cylinders are used care should be taken to ensure change-over from one cylinder to another. It should, for example, be u to trundle a fresh cylinder through a ward in the middle of the nig

... is likely to become exhausted before ...

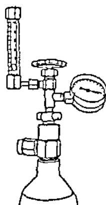


Fig 27.—Valve and flow-meter for administration of oxygen

(By courtesy of Coxeters)

should be some means of measuring and controlling the rate of flow. A simple flow-meter, together with a fine adjustment valve, is therefore necessary. A simple and compact form of valve and flow-meter is illustrated in Fig 27. The cost of such an apparatus is about £5. Without a flow-meter the rate of delivery of the gas is mere guesswork, and no apparatus for administering oxygen can be efficient in these circumstances. Oil must never be used to lubricate flow-meters and reducing valves owing to the danger of fire or explosion.

Arrangements can be made for oxygen therapy to be given in domiciliary practice, but the occasions on which this is either necessary or desirable are few. It is obviously difficult to maintain an adequate supply of oxygen in a private house, and when a patient really requires oxygen the risk of inadequate treatment at home is usually greater than the risk of moving him to hospital. Most ambulances are now equipped for oxygen to be given on the journey.

INDICATIONS FOR OXYGEN THERAPY

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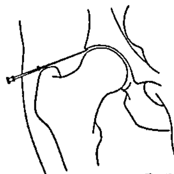


FIG 24.—*Hip joint* From a point immediately proximal to the mid-point of the upper border of the greater trochanter, the needle passes medially and slightly cranially, along the neck of the femur

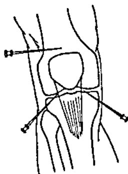


FIG. 25.—*Knee joint.* The needle may pass from either the medial or the lateral side (1) into the suprapatellar pouch, or (2) into the joint on either side of the ligamentum patellæ



FIG. 26.—*Ankle joint* From a point immediately distal to the tip of either malleolus, the needle passes cranially, and towards the median line of the tibia, between the malleolus and the talus.

JAMES LEARMONTH.
H. A. F. DUDLEY.

OXYGEN THERAPY

Oxygen supplied for medical use is specially prepared so as to be free of toxic constituents. Cylinders are available both of pure oxygen and of oxygen containing from 5 to 10 per cent. of carbon dioxide. These carbon dioxide-oxygen mixtures were introduced in the belief that it was sometimes advantageous to stimulate respiration by increasing the carbon dioxide content of the alveolar air, but it is now considered that such stimulation is seldom either necessary or desirable. In some patients the addition of carbon dioxide may stimulate respiration so violently as to cause severe distress. Others, whose respiratory centres are depressed by anoxia or by drugs, or whose lungs are grossly diseased, may be unable to increase their pulmonary ventilation sufficiently in response to the inhalation of carbon dioxide to keep the tension of this gas in the blood within normal limits If its administration is continued in such cases respiratory acidosis will develop

In most hospitals there are adequate facilities for the supply of oxygen. In an increasing number pipe-lines from a central bank of cylinders carry oxygen to the operating theatres and to individual beds in the wards. In many hospitals, however, the position is still unsatisfactory. Problems are, of course, most likely to arise in those without a piped oxygen supply. The stock of cylinders may be too small to cover emergency requirements, or a sufficiently careful check may not be kept on their content of oxygen with the result that only empty or half-empty cylinders are available for the treatment of a seriously anoxic patient.

When individual cylinders are used care should be taken to ensure a smooth change-over from one cylinder to another. It should, for example, be unnecessary to trundle a fresh cylinder through a ward in the middle of the night. If the

cylinder in use is likely to become exhausted before the morning a reserve one should be at the bedside before the patient settles down to sleep.

Whether a piped oxygen supply is available or individual cylinders are used, it is essential that there should be some means of measuring and controlling the rate of flow. A simple flow-meter, together with a fine adjustment valve, is therefore necessary. A simple and compact form of valve and flow-meter is illustrated in Fig. 27. The cost of such an apparatus is about £5. Without a flow-meter the rate of delivery

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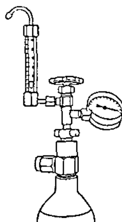


FIG 27—Valve and flow-meter for administration of oxygen
(*By courtesy of Coxeters*)

INDICATIONS FOR OXYGEN THERAPY

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accurate but less popular term—*hypoxia* Anoxia is a state in which the amount of oxygen reaching the tissues is inadequate for their needs Anoxia has a variety of causes, not all of which can be remedied by the inhalation of air containing a high concentration of oxygen For example, in anæmic anoxia, which is due to a reduction in the total amount of functioning hæmoglobin, the blood leaves the lungs oxygenated almost to the limit of its capacity and its oxygen content cannot therefore be raised significantly by increasing the concentration of oxygen in the inspired air. This type of anoxia occurs in severe anæmia and in ca[illegible] valueless; in the latter, [illegible] immediate relief of anox[illegible] hæmoglobin it indirectly relieves the anoxia

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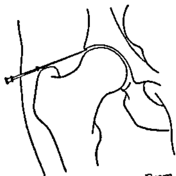


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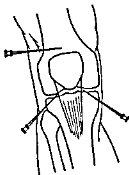


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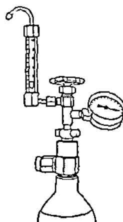


Fig 27 —Valve and flow-meter for administration of oxygen
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cardiovascular system whereby an insufficient amount of blood, and hence of oxygen, reaches the tissues. In this condition the tissue cells extract an excessive amount of oxygen from the capillary blood, and the venous blood thus contains a much greater amount of reduced hæmoglobin than in normal subjects This type of defect cannot be effectively corrected by oxygen therapy

the nostrils; the apparatus being, in effect, a double nasal catheter. This apparatus is more comfortable and efficient than the simple nasal catheter, and is quite cheap.

With both types of nasal catheter the rate of oxygen flow should be 6 litres per minute, which will normally double the oxygen content of the alveolar air. A lower rate is liable to be ineffective and higher rates are poorly tolerated. Even at a rate of six litres per minute the patient may experience some discomfort from the force and drying effect of the oxygen stream on the nasopharyngeal mucous membrane. This discomfort can be partly relieved by three simple measures: (*a*) the catheter should have several additional lateral openings cut on it to dissipate the force of the oxygen stream; (*b*) when a single catheter is used it should be inserted into the two nostrils alternately; (*c*) the oxygen should be humidified by bubbling it through water.

Oxygen Masks.—The type of mask first used in clinical practice was that designed in 1917 by Haldane, who introduced the principle of the oxygen reservoir bag. This entailed a considerable saving in the use of oxygen and the concentration of that gas in the alveolar air could be doubled by a rate of flow of less than 3 litres per minute as compared with 6 litres per minute with a nasal catheter. The Haldane mask was heavy and cumbersome and is now obsolete. The B.L.B. mask [illegible]

to add resistance to the airway and the bag acts as an oxygen reservoir during expiration, thus eliminating the waste which occurs with the nasal catheter. The B L.B mask is thus both fairly comfortable to the patient and economical of oxygen.

[illegible]

or unwilling to keep his mouth closed. The oro-nasal type is more efficient than the original Haldane mask, the oxygen content of the alveolar air being doubled by a flow rate of only 2 litres of oxygen per minute. Its present design, however, has the disadvantage, which may in certain circumstances be important, that the air in the re-breathing bag contains about 3 per cent. of carbon dioxide. In most patients this is harmless (some authorities consider it may even be beneficial), but in those with a seriously impaired respiratory reserve or who have pleuritic pain the stimulus to respiration so produced may be distressing.

[illegible]

between the mask and the bag, as in the original Haldane design. This type of mask is not yet in commercial production, but may be available in the near future.

In patients without severe emphysema the oro-nasal type of B.L.B. mask employing the re-breathing principle has, generally speaking, proved satisfactory. A flow rate of 4 litres per minute, which almost trebles the oxygen content of

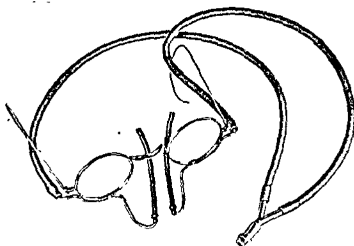




PLATE IA and B.—Tudor Edwards Catheter Carrier (spectacle frame type)
(British Oxygen Gases Ltd.)

[To face page 884



PLATE IIA —B L B Mask (nasal type)
(British Oxygen Gases Ltd.)



PLATE IIB —B L B Mask (oro-nasal type)
(British Oxygen Gases Ltd)



PLATE III.—Disposable plastic mask ("Polymask")
(*British Oxygen Gases Ltd.*)

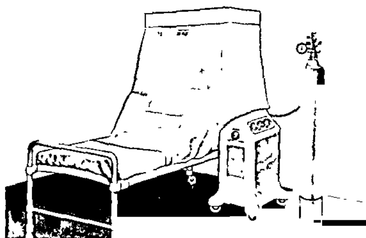


Plate IV.—Oxygen Tent with electrically operated refrigeration unit.

oxygen is administered with the unmodified B.L.B. mask to patients with severe emphysema, particularly those with retention of carbon dioxide in the blood, it should either be given intermittently (15 to 30 minutes per hr.) at the usual flow rate, or continuously at a reduced rate (1 to 2 litres per min). It is safer, however, in such cases to use a mask which does not employ the re-breathing principle or, alternatively, a nasal catheter.

For sterilization of B.L.B. masks the makers recommend that each part be washed with soap and water and rinsed before boiling for three minutes. It is advisable to support the rubber parts on a wire screen to prevent their coming into contact with the overheated bottom of the utensil in which they are immersed. After boiling they are hung up to dry. No antiseptic should be used.

Recently a disposable plastic mask ("Polymask") supplied by the British Oxygen Company has appeared on the market (Plate III) It also employs the

the face, but while this makes it more extravagant of oxygen it also prevents the accumulation of carbon dioxide in the re-breathing bag and the overstimulation of respiration which may result. With a rate of flow of 6 litres per minute it

of administering oxygen at present available and is particularly suitable for children, although a few of them find the close confinement frightening at first.

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a mask or a nasal catheter, and to whom an oxygen tent may afford the only chance of recovery.

The oxygen tent (Plate IV) forms a closed canopy over the head of the patient's bed, sealed by the mattress and bedclothes Oxygen flows into this enclosed space from a cylinder or pipe-line, but because the heat generated by the patient cannot escape to the atmosphere at the normal rate, the oxygen must be cooled sufficiently to keep the internal temperature of the tent comfortable. Until recently this could be achieved only by passing the oxygen through a chamber containing ice, the supply of which had to be replenished every 1 to 2 hours. However, an "iceless" oxygen tent has now been introduced, in which electrical refrigeration is employed Because of the heavy capital cost of the equipment it is the practice in many hospitals to hire oxygen tents from manufacturers as they are needed, but this, too, is expensive, and such a step should not normally be taken until it is clear that satisfactory results cannot be obtained by simpler and less costly methods.

The manufacturers who supply the tents issue detailed instructions for use. In addition, they usually send a technician to instal each tent and a on its maintenance. The following points, however, should be emphasized

(1) In order to increase the concentration of oxygen to a therapeutic l the tent should be flushed with oxygen for fifteen to twenty minutes before flow is reduced to a constant level of 4 to 8 litres per minute.

(2) After nursing attention has been given via the special flaps provided the sides of the tent, the concentration of oxygen should be restored by flushin for three to five minutes

(3) A constant watch must be kept on the temperature within the tent by means of a thermometer. The regulator should be adjusted to maintain the temperature at, or slightly below, that of the ward. Where *ice* is used for cooling the ice cabinet must be kept full.

(4) In view of the danger of fire, the tent should be at a safe distance from naked flames, and smoking should be prohibited in the immediate vicinity. Nothing that might provoke spontaneous combustion—electric heating appliances, bell pushes, etc. should be used inside the tent.

Duration of Oxygen Therapy.—Except when there is a danger of carbon dioxide retention in the blood, as in patients with severe emphysema, oxygen should always be administered *continuously*. When it is being given to correct anoxæmia of recent origin, for example in acute pneumonia, it should be continued until cyanosis no longer reappears after administration is discontinued for ten to fifteen minutes

In cases where the indication for oxygen therapy is a sudden increase in the degree of chronic anoxæmia, it is more difficult to know when to stop treatment. In such patients the reappearance of cyanosis after temporary withdrawal of oxygen is not an absolute indication to continue treatment, but the return of other symptoms and signs of anoxæmia, such as mental confusion, sweating and a rise in pulse rate or blood pressure, strongly suggest that oxygen is still needed.

I. W. B. GRANT.

PRINCIPLES OF PRESCRIBING

THE CARE of a sick person involves many procedures which do not necessarily include the administration of drugs or medicines. Throughout this volume emphasis is put upon the management and treatment of the patient as a whole, and drug administration for that patient may be of the least or of the greatest importance

When drugs are used, therefore, it is incumbent upon the practitioner to be conversant with their pharmacological action and their expected effect upon the patient to whom they are to be given Above all, he must know how best to assess and measure the drug's effect, realizing that considerations not applicable in a laboratory have to be taken into account. The subjective appraisement by the patient of an effect has to be balanced against the objective evidence of measureable change, be it, for example, blood count, pulse rate, weight, or urine volume. The doctor conducting the trial is equally liable to error, and he must ensure that bias, conscious or not, and possible anticipation of the expected effect do not influence the quality and value of his observations.

The physician therefore must always be critical in his use of drugs and of the results which it may be tempting to ascribe to these drugs. Many important new remedies are subjected to properly controlled clinical trials before becoming generally available. Nevertheless, many remedies are used which have not been thus investigated, and when this is done the much publicized claims of the manufacturers or promoters may be discovered to be ill-founded.

In all civilized countries doctors conform to certain general principles when writing prescriptions the pharmacist is instructed to supply the drug made up in a specified form and quantity for a particular patient Adequate directions on the package, box or bottle should indicate the manner in which the drug is to be used. These directions should answer clearly four questions how much, how often, when and in what manner is it to be taken or applied?

Certain conventions and customs govern the form of the prescription in order that there should be no confusion, and therefore no danger, regarding the nature of the drug, the dose, or mode of use. Further, the distribution and use of certain drugs is limited by legal and statutory regulations , under the conditions applying to the National Health Service in the United Kingdom, further restrictions are applied to the content of a doctor's prescription

The doctor is responsible for the accuracy of his prescription, and although it is customary for pharmacists in doubt about a script to confirm by direct reference to the doctor that the prescription does in fact represent his intention, this is only a courtesy and not an obligation

The pharmacist's duty is to dispense the drugs which the doctor feels are the most suitable for his patient Most of the doses which he dispenses do no normally exceed the maximum quantities recommended in the British Pharma copœia. It is therefore important that the doctor should discharge his dut scrupulously and exercise the utmost care in prescribing, always initialling dos which exceed B.P. doses When this practice is adopted, the pharmac recognizes that the dose represents the true intention of the doctor, and it is duty to dispense that prescription.

Form of Prescription.—The heading of the prescription should include the doctor's address (except in a National Health Service prescription on the official form), the date, and the patient's name and address. The main part of the script is preceded by the symbol "R" which is an abbreviation for the Latin "recipe" or "take".

The prescription then lists the drugs to be dispensed and the quantity of each to be taken by the patient at each dose. Then follow the instructions t pharmacist regarding the total quantity of the drug or drugs to be dispensa the final section of the script specifies, under the heading "Sig." (an abbrev for the Latin "signetur", "let it be labelled") the instructions to be giv the patient on the label of the box or bottle.

It may seem unnecessary to stress the necessity for legibility in ha writing. Nevertheless, the prevalence of writing and signatures which can be deciphered still causes inconvenience and delay to pharmacists and patien A prescription is only acceptable when signed by a doctor, and the pharmaci should be in a position to identify the writer and check the validity of a prescrip tion by reference to the Medical Register, or to the doctor himself.

It is customary, although not legally obligatory, to add medical qualifications at the foot of a prescription, after the signature.

Legal Requirements in Prescribing.—The nature and quantity of drugs that can be used in medicine are limited by certain legal qualifications. In the first place there are, of course, regulations that prevent potential poisons from being obtained by the public without due authorization, and further legislation specifies precautions to protect the patient and general community.

Pharmacy and Poisons Act, 1933.—This Act and the regulations issu under the Poisons Rules, 1952, and subsequent amendments, govern an control the sale and distribution of poisons throughout the country. The poison list has two parts: those drugs in Part I can only be sold by pharmacists, but Part II poisons can also be sold by listed sellers of poisons. Most of the drugs of importance which are used in therapeutics are listed as Part I poisons.

The rules issued under the Act also include a number of Schedules specifying those drugs affected by further restrictions and exempted from certain provisions of the Act. Of these, Schedules I and IV are of interest to doctors: Schedule poisons, most of which are in Part I of the Poisons List, can be sold without prescription provided that the vendor knows the buyer, who must sign an appropriate entry in a poisons book; Schedule IV lists those drugs from Schedule I which require a signed medical prescription conforming to certain criteria.

The purpose of the Schedule IV regulations, which are those which primarily affect medical practitioners, is to prevent the public having uncontrolled access to potentially dangerous substances such as sulphonamides, barbiturates or amphetamine. It is becoming customary for similar new drugs to be categorized in Schedule IV if undue risk may attach to their indiscriminate use. The prescription must include all the particulars specified earlier; and the total quantity of the active agent, or of the official preparation, to be dispensed must be stated. Private prescriptions may not be repeated unless specific instructions to the dispenser are given. A National Health Service prescription on the regulation form (E.C. 10) cannot be dispensed more than once.

The Dangerous Drugs Acts (D.D.A. 1951) are concerned with the surveillance of the manufacture, importation and ultimate distribution of those drugs, the

use of which is most likely to lead to addiction Obvious examples are opium and many of its derivatives, cocaine, Indian hemp and synthetic analgesics like pethidine and methadone Many of the regulations are designed to frustrate international trafficking in these drugs, and subsidiary legislation is from time to time introduced to supplement existing law, usually as the contribution of this country towards the execution of the policies of the World Health Organisation.

The Dangerous Drugs Acts affect the doctor in that they lay down precise rules governing prescriptions for these drugs, rules similar in their scope to those affecting drugs listed in Schedule IV, and very detailed regulations ensure that supplies of dangerous drugs are controlled from the time of manufacture until used by the patient

The Pharmacy and Medicines Act, 1941, specifies that drugs and preparations included in the British Pharmacopœia and British Pharmaceutical Codex may only be supplied by registered medical practitioners, dentists and pharmacists, and by those persons licensed to do so before 1941. It is furthermore made illegal to advertise a drug which claims to be a cure for certain diseases like diabetes, epilepsy, tuberculosis and some other conditions.

A most important step to abolish secret and, usually, ineffective remedies was achieved by this Act, which also stipulates that any medicine must be suitably labelled on the container to indicate the names and quantities of its constituents Unfortunately this does not apply to drugs dispensed from a prescription, and many boxes of tablets and bottles of medicine cannot be identified with certainty In any such case of doubt, the drug should be discarded and destroyed If the letters N P (nomen proprium) be added to a prescription by the doctor, the dispensing pharmacist will include the name of the drug on the appropriate label, a sensible practice which might well be more generally adopted.

The Penicillin Act, 1947, and its regulations ensure that penicillin and most other antibiotic substances can only be obtained by the public on the authority of a prescription.

The Therapeutic Substances Act, 1925, provides for official supervision of the manufacture, activity, sterility, etc , of a number of substances in which great care is required to ensure the production of reliable preparations.

National Health Service Prescribing.—Prescriptions for patients being treated under the regulations of the National Health Service have to be written on the official forms (E.C 10), which, however, cannot be used for private patients. Doctors are asked to use a separate prescription for each patient and not to include more than two items on any one form.

A doctor obtains his own personal requirements in Scotland by presenting a " stock order form " (E C 101 Scotland) to the pharmacist who supplies him and is reimbursed by the Executive Council In England and Wales personal requirements are paid for from a fund based on the size of the doctor's list of patients. Somewhat different regulations apply to the provision of drugs in the relatively few remaining dispensing practices

There is no absolute restriction on the prescribing of any drug which a doctor considers to be in the best interests of his patient, and doctors are not subject to any form of central direction as to what may or may not be prescribed There are, however, certain relative restrictions qualifying prescribing habits. A doctor may be called upon to justify his prescribing to his colleagues on the

Local Medical Committee if he appears to have prescribed excessively, or if he has prescribed substances which are not specified as drugs, which have not been shown to be of therapeutic value, or which have been advertised to the public.

Guidance to doctors regarding what should and what, if possible, should not be prescribed is given in a number of publications. In the first place, a *Joint Sub-committee on Definition of Drugs* has submitted a series of reports in which substances held to be foods, toilet preparations or disinfectants are defined. These reports have no statutory authority, but the existence of such reports is of assistance to Executive Councils, who may, after reference to the Local Medical Committee, recover from a doctor the cost of any substance which he has prescribed and which has been held not to be a drug. It can be well understood that it is frequently a matter of some difficulty to decide when, for example, a skin ointment becomes a toilet preparation and not a drug, or when certain "invalid foods" can be regarded as drugs that can be legitimately prescribed.

The Joint Committee on Prescribing, which is an independent professional committee of doctors and pharmacists, has held that since the responsibility for prescribing rests chiefly with the doctor, it is therefore undesirable that drugs advertised direct to the public should be prescribed on the statutory form E.C. 10. Lists of these drugs are published from time to time. Occasionally a manufacturer may provide an ethical preparation which is categorized as prescribable on Form E.C. 10, and then proceed to offer the identical preparation direct to the public under a different trade-name. In that event the Joint Committee—which is concerned with actual substances as distinct from *names*—must presumably rescind categorization of the drug or decline to allocate it to a category according to circumstances.

Drugs and preparations included in the British Pharmacopœia, British Pharmaceutical Codex and National Formulary are freely prescribable (unless defined as foods, etc.). The booklet *Proprietary Medicines classified by the Joint Committee on Prescribing* separates those proprietary preparations which are of value (category 1) and which are freely prescribable, from those which are of no proven therapeutic value and which should not be prescribed unless the practitioner is prepared to defend their use (categories 5 and 6). The booklet does not list the drugs classified in categories 2, 3 and 4, but they may all be prescribed under the National Health Service regulations, although the Committee regard the preparations in these groups as not necessarily therapeutically superior to standard preparations. In many instances, however, although a drug may be given a standard specification and be included in the British Pharmacopœia or National Formulary, it is only available in the market in the form of the proprietary preparations manufactured by individual pharmaceutical houses. In such circumstances pharmacists dispensing a prescription for the standard preparation have no alternative but to provide the proprietary drug. The latter is usually pharmacologically and chemically identical with the standard specification but may have, in addition, some colouring or flavouring agent which disqualifies it from being described as a standard preparation. A pharmacist is not permitted to dispense the equivalent standard official drug if presented with a prescription for the proprietary preparation, although such a procedure would often fulfil the doctor's therapeutic aims.

The nature and quantity of the drugs that a doctor prescribes for the patients on his list are kept under review by the Executive Councils, and occasionally examples of what appear to be excessive and unjustifiable prescrib-

ing are referred to the Local Medical Committee. The latter may recommend, after inquiry, that a sum of money should be recovered by the Executive Council from the doctor concerned

A great deal of helpful information is given to doctors in *Prescribers' Notes*, publications issued in loose-leaf form from time to time by the Ministry of Health and the Department of Health for Scotland. Succinct and sensible advice is given on prescribing practice generally, on current costs of drugs and appliances, and about the introduction of new preparations as they become available for general prescription

Nomenclature of Drugs.—Drugs should always be described, if possible, by their official names, unless it is desired for a special reason that a particular proprietary preparation be dispensed The "official" name is that name applied to the drug in the monographs in the British Pharmacopœia (B P.), the British Pharmaceutical Codex (B P.C), the National Formulary (N.F.) or, if the drug is not included in such volumes, the approved name bestowed upon it by the Nomenclature Committee of the British Pharmacopœia Commission. Lists of such approved names are periodically issued by the Commission, and a committee of the World Health Organization tries to ensure uniformity of [illegible]

[illegible] Formulary may be expected to do so eventually The pseudo-Latinization of the names of new drugs is quite absurd and unnecessary, and is a relic of another era. Nowadays there is no tenable argument for the use of Latin in any part of a prescription.

Dosage and Quantities of Drugs to be Prescribed.—When possible, dosage should be specified in metric measures, as this is now becoming more generally a[illegible] in metric [illegible] however, [illegible] been so dispensed It has been officially determined that by 1963 even they will be officially described in terms of the metric system. Increasing quantities of metric containers for liquid medicines, lotions, etc., are becoming available, and this will facilitate the adoption in this country of the more sensible and convenient system which has always been the practice throughout much of the rest of the world.

Solutions and ointments with numerous constituents should always be prescribed in terms of metric measures, as much confusion and inaccuracy may result from unnecessary and misguided attempts to combine solid grains with fluid ounces

A convenient table of approximate equivalent values for imperial and metric measures appears on p. 900

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because shorter intervals involve increasing costs due to dispensing charges, and inconvenience due to frequent visits to the doctor. Dangerous drugs such as barbiturates should be supplied in the smallest reasonable amount for the circumstances; and expensive drugs which are being used for the first time should be ordered in small quantities

Mixtures and lotions should be supplied in 250 ml. or 500 ml. quantities (8 to 16 fluid ounces). Eye drops are dispensed in 8 ml. and ear and nose drops in 15 ml bottles (quarter to half fluid ounce bottles). The amount of an ointment prescribed depends on the area to be covered—perhaps 5 g. for an eye ointment, and 50 to 100 g. when extensive areas of the body have to be covered.

Selection of Preparation to be Prescribed.—A drug can usually be administered by mouth, and this should be the route of choice unless it is imperative that it be injected, either because it is unpalatable or inactive when taken by mouth, or because a different speed of action is required.

Such a medicine should, if possible, be given as a dry preparation, as a tablet or in a capsule, rather than as a mixture, tincture, elixir, etc. Tablets and capsules are far more convenient for both pharmacist and patient, they are a more accurate way of giving drugs, and are often cheaper with a lower dispensing fee. Only exceptionally is a mixture necessary; sometimes drugs cannot be dispensed as solids because of their physical properties; occasionally, also, drugs intended for children are more acceptable in a suitably flavoured liquid vehicle. Nevertheless, over two hundred million prescriptions are written annually under the National Health Service, and of these 24 per cent. are still for mixtures, a percentage so high that it suggests the influence of outworn conventions.

The great majority of the drugs and preparations used nowadays are standardized and defined in the British Pharmacopœia (1953) and the current Addendum (1955), but the British Pharmaceutical Codex (1954) and the National Formulary (1957) list some substances and compound preparations not included in the B.P. Individual and specially compound preparations for particular patients are seld[illegible] form[illegible] to [illegible] tha[illegible] pre[illegible] mixtures, powders, ointments, etc., are saved compared to [illegible]

There are few occasions when it becomes necessary to prescribe more than one drug at a time, and when it is necessary to do so, each drug is given for a specific purpose. The days of prescriptions containing a multiplicity of ingredients are ended, and there is no justification for the perpetuation of polypharmacy. Examples of true synergism are hard to find, and most of the alleged examples merely exemplify the additive rather th[illegible] of such drugs. It is usually pref[illegible]

Many of the most valuabl[illegible] ceutical manufacturing hous[illegible] proprietary form. They can [illegible] used quite freely, and should be so prescribed when, as occasionally occurs, the proprietary preparation is cheaper than the official equivalent. Further, as new drugs become established there is inevitably an interval before they receive the recognition implied by inclusion in the British Pharmacopœia or National Formulary. If shown to be of value, these proprietary preparations should naturally be freely used.

It is part of the pharmacist's business to make medicines palatable, but there is rarely any occasion to compete with the confectioner, though some latitude is desirable when he is dispensing for young children. In brief, it is fair to recommend a critical attitude towards the prescribing of proprietary preparations. Many of the claims made in the advertisements distributed to members of the medical profession are not in fact justifiable, and the drugs may not be as useful or as therapeutically effective as the manufacturers would have the doctor believe. There is often an acceptable and less expensive analogous standard preparation. The prescriber must always retain his critical faculties and should scrutinize carefully the evidence offered by manufacturers purporting to prove the therapeutic value of new preparations

A glossary on p. 895 lists the proprietary equivalents of those drugs described in this book by their approved or official names In a few instances, although the drug may be prescribed under its approved name, it can only be procured in its proprietary form

The Cost of Drugs and Prescriptions.—Under present conditions in the National Health Service the pharmaceutical services cost over £50,000,000 annually, about 10 per cent of the gross cost of the Service. Little over half of this sum covers the cost of the actual ingredients of the prescriptions issued, the balance representing dispensing fees, pharmacists' profit, allowance for containers, etc. It is therefore important to appreciate how the costs of prescription are calculated

The pharmacist is repaid by the Health Service in respect of a prescriptio in the following way: he receives payment for the basic cost of the ingredien which is the sum listed in the *Drug Tariff* This is a publication issued by Health Service authorities which lists the cost of basic drugs, applian dressings, etc. It also details the procedure for the costing of proprie preparations These prices are increased by 25 per cent, calculated on total cost of ingredients due to the pharmacist at the end of each month, this represents the oncost, or profit, to the pharmacist The Drug T applicable in England and Wales differs from that used in Scotland. pharmacists north of the border are remunerated at a different rate A tainer allowance of twopence is paid for each prescription, finally the dispensing charge, the size of which is calculated differently in England Scotland, and is dependent upon the type of preparation prescribed example, one shilling (1s 2d in Scotland) is paid for the dispensing tablets, or five shillings for the extemporaneous preparation of twelve a of a sterile solution.

There is a charge to the patient of one shilling for each item on a pre by which the State recovers a fraction of the cost of the pharmaceutical The total cost of a prescription to the Health Service can be several although the actual ingredients may cost only a few pence, and it is cheaper for the patient and for the Health Service for small quantitie drugs to be bought on an ordinary prescription and not on form E. the case of expensive drugs, the basic ingredient charge may comple ... and the practitioner should always be aware of the ... omic to prescribe inexpensive dru ... nged period, as the over

issue periodically to practitioners a booklet, called in Scotland *Costs of some Commonly Prescribed Drugs*, which gives full details of the actual cost to the Health Service of many standard preparations contained in the National Formulary and British Pharmaceutical Codex, and also the comparative costs of equivalent or similar proprietary preparations.

These publications provide invaluable safeguards against unnecessary and extravagant prescribing. Standard preparations are usually but by no means invariably cheaper than proprietary equivalents, but a more attractive pharmaceutical presentation may, as has already been noted, compensate for a slight additional cost of the latter.

Undoubtedly the greatest economy in prescribing can be effected by really careful thought as to the necessity, in the first place, for any drug administration at all, the most suitable and least costly preparation to use, and the most sensible and economical quantity of the drug to order for the patient. Drugs should be, and usually are, solely prescribed so that the patient may benefit from their pharmacological effect. When a drug is prescribed purely as a placebo—an admission usually that it is not expedient or advisable that time be spent on explanation and reassurance to the patient—an inexpensive and safe preparation should be selected.

A. G. MACGREGOR.

GLOSSARY

Glossary showing proprietary equivalents of drugs mentioned in this book by their official or approved name

Approved Name	*Proprietary Preparations*
Acetarsol	Stovarsol
Acetazoleamide	Diamox
Acetylsalicylic acid, soluble	Regaspirin; Solprin
Adrenal cortical extract	Eschatin; Eucortone
Amethocaine hydrochloride	Anethaine; Decicain
Amethopterin	Methotrexate
Aminophylline	Cardophyllin
Amiphenazole	Daptazole
Amodiaquine hydrochloride	Camoquin
Amphetamine	Benzedrine
Amphetamine sulphate	Amphamed, Benzedrine sulphate
Amylobarbitone	Amytal
Amylobarbitone sodium	Dorminal; Sodium Amytal
Aneurine hydrochloride	Benerva; Betalin
Antazoline	Antistin, Histostab
Barbitone	Veronal
Barbitone sodium	Medinal, Veronal sodium
Bemegride	Megimide
Benethamine penicillin	Benapen
Benzalkonium hydrochloride	Roccal
Benzathine penicillin	Dibencil; Eskacillin; Neolin; Penidural; Permapen
Benzhexol hydrochloride	Artane, Pipanol
Benzylpenicillin	Crystapen
Bismuth glycollylarsanilate	Milibis
Bismuth salicylate	Bisantol
Bismuth sodium tartrate	Sobita
Bromethol	Avertin
Busulphan	Myleran
Butobarbitone	Soneryl
Calciferol	Ostelin, Radiostol
Carbachol	Moryl, Doryl
Carbarsone	Leucarsone
Carbimazole	Neo-mercazole
Carbutamide	Bucrol
Cetrimide	Cetavlex; Cetavlon
Chiniofon	Quinoxyl
Chloral hydrate	Somnos; Welldorm tablets
Chloramphenicol	Alficetyn; Chloromycetin

Approved Name	Proprietary Preparations
Chlorcyclizine hydrochloride	Di-paralene; Histantin
Chloromerodrin	Mercloran; Neohydrin
Chloroquine phosphate	Aralen; Avloclor; Resochin
Chloroquine sulphate	Nivaquine
Chloroxylenol	Dettol
Chlorpromazine hydrochloride	Largactil
Chlortetracycline	Aureomycin
Corticotrophin	Acthar; Cortrophin
Cortisone acetate	Adreson; Cortelan; Cortistab; Cort
Cyanocobalamin	Anacobin; Bitevan; Cobastab; Cytamen; Euhaemon
Cyclobarbitone	Phandorm
Dapsone	Avlosulfon
Dehydrocholic acid	Certonin, Decholin; Dehydrocholin
Demecolcine	Colcemid
Deoxycortone acetate	Decortacetate; Percorten; Syncor
Dexamphetamine sulphate	Dexedrine
Dextran sulphate	Dexulate
Diethazine hydrochloride	Diparcol
Diethylcarbamazine citrate	Banocide; Ethodril; Hetrazan
Digitoxin	Crystodigin; Digitaline
Digoxin	Lanoxin
Dihydrotachysterol	AT 10
Di-iodohydroxyquinoline	Diodoquin; Embequin
Dimenhydrinate	Dramamine
Dimercaprol	BAL
Dimethyl phthalate	Mylol; Sketofax
Diphenan	Butolan; Oxylan
Diphenhydramine hydrochloride	Benadryl
Disulfiram	Antabuse; Cronetal
Dyflos	DFP
Edetic acid	Versene acid
Ergotamine tartrate	Femergin
Erythromycin	Erythrocin; Ilotycin
Ethinyloestrodiol	Estigin; Ethidol; Ethin-oestryl; Eticyclin; Lynoral
Ethisterone	Gestone oral; Lutocyclin; Oraluton; Progestoral
Ethopropazine hydrochloride	Lysivane
Ethyl biscoumacetate	Tromexan
Ferrous gluconate	Fergon, Ferlucon; Ferronicum
Ferrous succinate	Ferromyn
Ferrous sulphate	Fersolate
Folic acid	Folvite
Gamma benzene hexachloride	Gammexane; Lorexane

Approved Name	*Proprietary Preparations*
Heparin	Liquemin; Pularin
Hexamethonium tartrate	Vegolysen T
Hexobarbitone	Cyclonal; Hexanastab oral
Hexoestrol	Synthovo
Hyaluronidase	Hyalase; Rondase
Hydrallazine hydrochloride	Apresoline
Hydrocortisone	Cortril; EF-Cortelan Hydrocortistab; Hydro-Adreson; Hydrocortisyl
Hyoscine butylbromide	Buscopan
Insulin zinc suspension	Insulin Lente
Insulin zinc suspension (Amorphous)	Insulin Semilente
Insulin zinc suspension (Crystalline)	Insulin Ultralente
Iron dextran complex	Imferon
Isoniazid	I.N H., Neumandin; Nydrazid; Pycazide, Rimifon; Vazadrine
Isoprenaline sulphate	Neo-epinine
Isoprenaline hydrochloride	Isupren
Khellin	Benecardin, Viscardam
Leptazol	Phrenazol
Lucanthone hydrochloride	Miracil D, Nilodin
Mecamylamine	Inversine
Mepacrine hydrochloride	Quinacrine
Mepacrine methanesulphonate	Quinacrine soluble
Mephenesin	Myanesin, Tolseram
Mepyramine maleate	Anthisan
Mercaptomerin sodium	Thiomerin sodium
Mercaptopurine	Puri-Netol
Mersalyl	Salygran
Methacholine chloride	Amechol, Mecholyl chloride
Methadone hydrochloride	Physeptone
Methanthelinium bromide	Banthine
Methimazole	Mercazole, Tapazole
Methoin	Mesontoin
Methylamphetamine hydrochloride	Methedrine
Methylcellulose	Celevac; Cologel, Melozet
Methylpentynol	Oblivon, Somnesin
Methyltestosterone	Glosso sterandryl; Oraviron; Perandren linguets; Sublings Methytestosterone
Mustine hydrochloride	Nitrogen mustard
Nalorphine hydrobromide	Lethidrone
Neomycin	Neomin
Neostigmine	Prostigmin
Nikethamide	Anacardone; Coramine; Corvotone, Nikamide

Approved Name	*Proprietary Preparations*
Chlorcyclizine hydrochloride	Di-paralene; Histantin
Chloromerodrin	Mercloran; Neohydrin
Chloroquine phosphate	Aralen; Avloclor; Resochin
Chloroquine sulphate	Nivaquine
Chloroxylenol	Dettol
Chlorpromazine hydrochloride	Largactil
Chlortetracycline	Aureomycin
Corticotrophin	Acthar; Cortrophin
Cortisone acetate	Adreson; Cortelan; Cortistab; Cortisyl
Cyanocobalamin	Anacobin; Bitevan; Cobastab; Cytamen; Euhaemon
Cyclobarbitone	Phandorm
Dapsone	Avlosulfon
Dehydrocholic acid	Certonin; Decholin; Dehydrocholin
Demecolcine	Colcemid
Deoxycortone acetate	Decortacetate; Percorten; Syncortyl
Dexamphetamine sulphate	Dexedrine
Dextran sulphate	Dexulate
Diethazine hydrochloride	Diparcol
Diethylcarbamazine citrate	Banocide; Ethodril; Hetrazan
Digitoxin	Crystodigin; Digitaline
Digoxin	Lanoxin
Dihydrotachysterol	AT 10
Di-iodohydroxyquinoline	Diodoquin; Embequin
Dimenhydrinate	Dramamine
Dimercaprol	BAL
Dimethyl phthalate	Mylol; Sketofax
Diphenan	Butolan; Oxylan
Diphenhydramine hydrochloride	*Benadryl*
Disulfiram	Antabuse; Cronetal
Dyflos	DFP
Edetic acid	Versene acid
Ergotamine tartrate	Femergin
Erythromycin	Erythrocin; Ilotycin
Ethinyloestrodiol	Estigin; Ethidol; Ethin-oestryl; Eticyclin; Lynoral
Ethisterone	Gestone oral; Lutocyclin; Oraluton; Progestoral
Ethopropazine hydrochloride	Lysivane
Ethyl biscoumacetate	Tromexan
Ferrous gluconate	Fergon; Ferlucon; Ferronicum
Ferrous succinate	Ferromyn
Ferrous sulphate	Fersolate
Folic acid	Folvite
Gamma benzene hexachloride	Gammexane; Lorexane

Approved Name	*Proprietary Preparations*
Heparin	Liquemin, Pularin
Hexamethonium tartrate	Vegolysen T
Hexobarbitone	Cyclonal; Hexanastab oral
Hexoestrol	Synthovo
Hyaluronidase	Hyalase, Rondase
Hydrallazine hydrochloride	Apresoline
Hydrocortisone	Cortril; EF-Cortelan Hydrocortistab, Hydro-Adreson; Hydrocortisyl
Hyoscine butylbromide	Buscopan
Insulin zinc suspension	Insulin Lente
Insulin zinc suspension (Amorphous)	Insulin Semilente
Insulin zinc suspension (Crystalline)	Insulin Ultralente
Iron dextran complex	Imferon
Isoniazid	I N H., Neumandin; Nydrazid; Pycazide; Rimifon; Vazadrine
Isoprenaline sulphate	Neo-epinine
Isoprenaline hydrochloride	Isupren
Khellin	Benecardin, Viscardam
Leptazol	Phrenazol
Lucanthone hydrochloride	Miracil D, Nilodin
Mecamylamine	Inversine
Mepacrine hydrochloride	Quinacrine
Mepacrine methanesulphonate	Quinacrine soluble
Mephenesin	Myanesin, Tolseram
Mepyramine maleate	Anthisan
Mercaptomerin sodium	Thiomerin sodium
Mercaptopurine	Puri-Netol
Mersalyl	Salygran
Methacholine chloride	Amechol, Mecholyl chloride
Methadone hydrochloride	Physeptone
Methanthelinium bromide	Banthine
Methimazole	Mercazole, Tapazole
Methoin	Mesontoin
Methylamphetamine hydrochloride	Methedrine
Methylcellulose	Celevac; Cologel; Melozet
Methylpentynol	Oblivon; Somnesin
Methyltestosterone	Glosso sterandryl; Oraviron; Perandren linguets; Sublings Methytestosterone
Mustine hydrochloride	Nitrogen mustard
Nalorphine hydrobromide	Lethidrone
Neomycin	Neomin
Neostigmine	Prostigmin
Nikethamide	Anacardone; Coramine; Corvotone; Nikamide

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Corticotrophin	Acthar; Cortrophin
Cortisone acetate	Adreson; Cortelan; Cortistab; Cortisyl
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Dapsone	Avlosulfon
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Dextran sulphate	Dexulate
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Diethylcarbamazine citrate	Banocide; Ethodril; Hetrazan
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Digoxin	Lanoxin
Dihydrotachysterol	AT 10
Di-iodohydroxyquinoline	Diodoquin; Embequin
Dimenhydrinate	Dramamine
Dimercaprol	BAL
Dimethyl phthalate	Mylol; Sketofax
Diphenan	Butolan; Oxylan
Diphenhydramine hydrochloride	Benadryl
Disulfiram	Antabuse; Cronetal
Dyflos	DFP
Edetic acid	Versene acid
Ergotamine tartrate	Femergin
Erythromycin	Erythrocin; Ilotycin
Ethinyloestradiol	Estigin; Ethidol; Ethin-oestryl; Eticyclin; Lynoral
Ethisterone	Gestone oral; Lutocyclin; Oraluton; Progestoral
Ethopropazine hydrochloride	Lysivane
Ethyl biscoumacetate	Tromexan
Ferrous gluconate	Fergon; Ferlucon; Ferronicum
Ferrous succinate	Ferromyn
Ferrous sulphate	Fersolate
Folic acid	Folvite
Gamma benzene hexachloride	Gammexane; Lorexane

Approved Name	*Proprietary Preparations*
Quinalbarbitone sodium	Seconal sodium
Quinidine iodobismuthate	Quinostab
Reserpine . . .	Qiesein; Reserpex; Sandril; Serpasil
Resins (Cation exchange)	Carbo-resin; Katonium; Resonium A
Riboflavine .	Beflavit
Saccharated iron oxide	Ferrivenin; Neoferrum intravenous
Sodium aminosalicylate .	Bactylan; Paramisan sodium
Sodium antimony gluconate	Triostam
Sodium aurothiomalate	Myocrisin
Sodium calciumedetate	Calcium versenate
Sodium stibogluconate	Pentostam
Solapsone	Sulphetrone
Stibophen	Fouadin
Stilbœstrol	Clinestrol; Neooestranol, Pabestrol
Streptomycin	Streptolin, Styzolin
Succinylsulphathiazole	Sulphasuxidine
Sulphacetamide	Albucid; Steramide
Sulphadiazine	Cremodiazine
Sulphadimidine	S-Mez; Sulphamezathine
Sulphafurazole	Gantrisin
Sulphapyridine .	M & B 693
Sulphathiazole	Cibazol; Thiazamide
Suramin	Antrypol, Bayer 205; Germanin; Fourneau 309;
Testosterone propionate	Perandren; Sterandryl; Testaform; Testoviron
Tetracycline .	Achromycin; Tetracyn
Thiosemicarbazone	Berculon A
Thiopentone sodium	Intraval sodium; Pentothal
l-Thyroxin	Eltroxin
Tolazoline hydrochloride	Priscol
Tolbutamide	Rastinon
Tretamine	Melamine; TEM, Triethanomelamine, Tri-Ethylene
Tricyclamol chloride	Elorine chloride; Lergine
Trimetaphan	Arfonad
Tripellennamine hydrochloride	Pyribenzamine
Troxidone	Tridione
Vasopressin tannate	Pitressin tannate
Vitamin K (Synthetic)	Menadione; Synkavit
Vitamin K_1 (Synthetic)	Konakion
Viomycin .	Viocin; Vionactane

Approved Name	Proprietary Preparations
Nitrofurantoin	Furadantin
Noradrenaline	Adrenor; Levophed
Oxyphenarsine hydrochloride	Mapharside
Oxyphenonium bromide	Antrenyl
Oxytetracycline	Terramycin
Pamaquin	Plasmoquine; Praequine
Pancreatin	Panar granules
Papaveretum	Omnopon
Penethamate hydroiodide	Estopen
Pentaerythritol tetranitrate	Mycardol; Peritrate
Pentobarbitone sodium	Nembutal
Pentolinium tartrate	Ansolysen
Pethidine hydrochloride	Dolantal
Phenadoxone hydrochloride	Heptalgin
Phenindione	Dindevan; Indema
Phenobarbitone	Gardenal
Phenobarbitone sodium	Gardenal sodium
Phenoxymethyl penicillin	Distaquaine V; Penavlon V; Penicillin V; V-Cil
Phenylbutazone	Butazolidin
Phenylephrine hydrochloride	Neophryn; Neosynephrine
Phenytoin sodium	Epanutin; Eptoin
Piperazine adipate	Entacyl
Piperazine citrate	Antepar; Helmezine
Piperazine tartrate	Veroxil
Polymyxin B	Aerosporin
Posterior Pituitary Injection	Pitoxylin
Prednisolone	Codelcortone; Deltacortril; Deltaefcortelan; Delta-stab; Di-Adreson-F; Metacortandrolone; Precortisyl; Ultracorten H
Prednisone	Decortisyl; Delta-cortelan; Delta cortone; Di-Adreson; Metacortandracin; Ultracorten
Primidone	Mysoline
Probenecid	Benemid
Procainamide hydrochloride	Pronestyl
Progesterone	Luteostab; Lutocyclin; Lutoform; Progestin; Proluton
Proguanil hydrochloride	Paludrine hydrochloride
Promethazine chlorotheophyllinate	Avomine
Promethazine hydrochloride	Phenergan
Propantheline bromide	Probanthine bromide
Pyridostigmine	Mestinon
Pyridoxine hydrochloride	Benadon
Pyrimethamine	Daraprim

Approved Name	*Proprietary Preparations*
Quinalbarbitone sodium	Seconal sodium
Quinidine iodobismuthate	Quinostab
Reserpine	Quesein; Reserpex; Sandril; Serpasil
Resins (Cation exchange)	Carbo-resin; Katonium; Resonium A
Riboflavine	Beflavit
Saccharated iron oxide	Ferrivenin; Neoferrum intravenous
Sodium aminosalicylate	Bactylan; Paramisan sodium
Sodium antimony gluconate	Triostam
Sodium aurothiomalate	Myocrisin
Sodium calciumedetate	Calcium versenate
Sodium stibogluconate	Pentostam
Solapsone	Sulphetrone
Stibophen	Fouadin
Stilbœstrol	Clinestrol, Neooestranol; Pabestrol
Streptomycin	Streptolin; Styzolin
Succinylsulphathiazole	Sulphasuxidine
Sulphacetamide	Albucid; Steramide
Sulphadiazine	Cremodiazine
Sulphadimidine	S-Mez, Sulphamezathine
Sulphafurazole	Gantrisin
Sulphapyridine	M & B 693
Sulphathiazole	Cibazol, Thiazamide
Suramin	Antrypol, *Bayer 205; Germanin; Fourneau 309;*
Testosterone propionate	Perandren, Sterandryl; Testaform; Testoviron
Tetracycline	Achromycin, Tetracyn
Thiosemicarbazone	*Berculon A*
Thiopentone sodium	Intraval sodium; Pentothal
l-Thyroxin	Eltroxin
Tolazoline hydrochloride	Priscol
Tolbutamide	Rastinon
Tretamine	Melamine, TEM, Triethanomelamine, Tri-Ethylene
Tricyclamol chloride	Elorine chloride; Lergine
Trimetaphan	Arfonad
Tripellennamine hydrochloride	Pyribenzamine
Troxidone	Tridione
Vasopressin tannate	Pitressin tannate
Vitamin K (Synthetic)	Menadione; Synkavit
Vitamin K_1 (Synthetic)	Konakion
Viomycin	Viocin; Vionactane

WEIGHTS AND MEASURES

Table of the approximate Equivalents used in this Book

0·5 Milligramme (mg.)	= $\frac{1}{120}$ grain (gr.)
0·6 " "	= $\frac{1}{100}$ " "
1 " "	= $\frac{1}{60}$ " "
5 " "	= $\frac{1}{12}$ " "
15 " "	= $\frac{1}{4}$ " "
30 " "	= $\frac{1}{2}$ " "
60 " "	= 1 " "
0·1 Gramme (g.) or Millilitre (ml.)	= $1\frac{1}{2}$ " "
0·3 " " "	= 5 " " or minims (min.)
0·5 " " "	= 8 " " " "
0·6 " " "	= 10 " " " "
1 " " "	= 15 " " " "
30 " " "	= 1 ounce (oz.) or 1 fluid ounce (fl. oz.)
1 Kilogramme (kg.)	= 2·2 pounds (lb.)

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4 Millilitres (ml.)	= 1 fluid drachm (fl. dr.)
16 " "	= $\frac{1}{2}$ fluid ounce (fl. oz.)
30 " "	= 1 " " (")
600 " "	= 1 pint (pt.) or 20 fluid ounces (fl. oz.)
1 Litre (l.)	= $1\frac{3}{4}$ pints (pt.)

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25 Millimetres (mm.)	= 1 inch (in.)
1 Metre (m.)	= 39 inches (in.)

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